A STUDY OF THE GASTRIC SECRETION OF HEALTHY AND ILL INFANTS IN THE FIRST YEAR OF LIFE.

Thesis presented by

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PREFACE

The work for this thesis was carried out in the Wards and Biochemical Laboratory of the Royal Hospital for Sick Children, Glasgow, and in the Nurseries of the Maternity Wards of the Glasgow Municipal Hospitals.

I wish to express my gratitude to Professor G.B. Fleming for suggesting this research and for his constant encouragement in carrying it through. I would also like to thank Dr.Finlay Ford, who very kindly placed material at my disposal in the Glasgow Municipal Hospitals. To Dr.H.E.C.Wilson I am indebted for advice in planning the biochemical work. I must also tender my thanks to the Sisters and nursing staff of all the wards, without whose co-operation, this work would not have been possible.

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INTRODUCTION

Historical Survey.

Scientists and philosphers of earlier times, interested in the problem of digestion, were handicapped by the lack of means of withdrawing gastric juice from the stomach of animals or human beings during life. Many of their ideas were theoretical, knowledge based on experimental evidence was scanty.

Robertson (88) states that Van Helmont, in 1648, wrote of an acid ferment in the stomach, responsible for digestion; he thought that the chemical activity was governed by invisible spiritual agencies. Borelli about the same time suggested that digestion was a mechanical grinding and crushing by the stomach, whereas Sylvius upheld the theory of chemical fermentation, though he discarded mystic and supernatural influences. In 1692, Virdet was reported to have killed animals to obtain their gastric juice for study. By the end of the 17th century, current opinion regarded digestion, either as an act of trituration, or a chemical action operating through fermentation via the saliva or through a secretion from the lining of the stomach.

Mettler (66) tells us that Boerhaave, an early 18th century physiologist, denied the acidity of the gastric juice, and considered the process in the stomach to be an incipient fermentation. Digestion was a solution of certain parts of the food in several juices, accompanied by motions of trituration in the

stomach. Haller, a pupil of Boerhaave, suggested that the succus gastricus was a neutral macerating fluid secreted by the arteries.

Réaumur, in 1752, made an important contribution to the knowledge of the physiology of digestion by his work on a kite. The bird swallowed hollow perforated tubes in which various foods had been placed, and when these tubes were vomited some time later, the food within was found to be partly digested, without any odour of putrefaction. He obtained pure gastric juice by inserting sponges in the tubes, and used this for in vitro experiments. He concluded that digestion was a process whereby food was dissolved by the gastric juice.

Reuss, in 1760, was the first person to study human gastric juice, obtaining it from people, who could vomit at will. Stevens, 17 years later, also investigated human gastric juice by methods similar to Réaumur's. They both agreed with Réaumur as to the solvent effect of gastric juice.

Spallanzani adopted and improved Réaumur's methods, and experimented on himself as well as on a variety of animals. After years of work, in 1783, he established the theory of the chemical process of digestion; he declared that gastric juice in health was entirely neutral; it was a solvent for edible substances in vivo and in vitro; it preserved animal matter from putrefaction at air temperature though dissolving it with the aid of heat.

An important observation was made by

Carminati in 1785. He noted that the juice in the stomach of carnivorae was acid after food had been eaten, but the fasting juice was not acid ... In 1800, Werner confirmed that in both carnivorae and herbivorae, the gastric contents were acid during digestion ... Young a few years later, experimenting on himself and on frogs, concluded that the acid was phosphoric acid.

Montegre, in 1812, stated that gastric juice and saliva were the same, and denied that gastric juice was a solvent. He said that it was neutral, and that any traces of free acid present in gastric contents, were due to incipient decomposition.

It remained for Prout in 1824 to prove that the acid of the gastric juice was free hydrochloric acid or muriatic acid. Gmelin and Tiedman working independently came to the same conclusion.

Beaumont published in 1833 his classical observations on Alexis St. Martin, who, as the result of a gun shot wound, developed a gastric fistula, through which gastric juice was readily obtained direct from the stomach. Beaumont confirmed Prout's discovery of the presence of hydrochloric acid in the stomach, and recognised that the essential elements of the gastric juice and the mucus secretion were separate. He studied digestion, both inside and outside the body, and demonstrated the continuation of the natural process when food was taken out of the stomach during chymification. He noted by direct observation, the great influence of mental

disturbances on digestion, and on the secretion of gastric juice. His work led Schwann, 3 years later, to the discovery of pepsin in gastric secretion.

In spite of this work, Claude Bernard and others held that the free acid secreted by the stomach was lactic acid, and that hydrochloric acid was formed by the action of lactic acid on the chlorides. In 1852, Bidder and Schmidt disposed once and for all of the lactic acid theory, and proved that hydrochloric acid was the free acid of the gastric juice; they showed there was an excess of chlorides present over that of the bases estimated, and this excess of chlorides was alone sufficient to account for the entire acidity of the gastric juice. Seventeen years later, Voit showed that the hydrochloric acid in the stomach, was derived from the chlorides in the blood plasms.

There was still no means whereby gastric contents could be directly obtained, except by vomiting or through a fistulous opening, but the introduction of the vulcanization of rubber in 1844 made rubber tubes practicable. Garrison (38) states that the principles and practical applications of the stomach pump were probably evolved before 200 B.C., but the instrument was used mainly in treatment. Boerhaave, in the early 18th century, mentioned its use in poisoning, and Monro Secundus in 1767 also recognised its use in such cases. John Heysham, in 1783, treated hysterical dysphagia by pushing down a tube, and John Hunter, 7 years later, used it to feed a patient with an oesophageal stricture. In 1869 Kussmaul

employed the stomach tube in a case of pyloric obstruction, but there is no note of any chemical examination of the gastric contents withdrawn.

The stomach tube was first used for diagnostic purposes by Von Leube in 1871, and twelve years later he made the first attempt to study the digestive and motor capacity of the stomach after a standardised meal. He gave the patient at midday, a test meal of beef bouillon, beef steak, pureed potatoes and one slice of bread; after 7 hours all the contents of the stomach were aspirated. The amount of residue withdrawn was measured, the degree of digestion noted, and the concentration of acid and pepsin determined. In using a standardised method he sought to obtain information on the motor and secretory function of the stomach that would be of diagnostic value in patients suffering from various disorders. In 1885, Ewald and Boas, and Riegel, introduced a similar type of meat and bread meal, but the single aspiration was made half to one hour after ingestion of the meal.

However, most other methods were superseded by the Test Breakfast of Ewald and Boas, introduced in 1886, and [illegible] still in use to-day. It gave information as to both the secretory and motor activity of the stomach and took precedence as a standard. In its original form, Ewald and Boas gave 35 gm. of white bread and 400 c.c. of water, but Hollander and Penner (50) report a wide variation in the components in use to-day. The meal may consist

of any one of the following solid foods, viz., bread, white bread, toast, sweetened rolls, crackers of various kinds, and all either buttered or unbuttered, and in quantities varying from 30 to 70 gm.; the accompanying fluid may be water or tea (without sugar or cream) 200 to 500 c.c.

In 1891, Hayem and Winter took matters a step further. They plotted curves of the free, total and combined acid of the fasting juice, and of specimens aspirated at thirty minute intervals after an Ewald - Boas Test Meal. Schule, 1895, carried out similar examinations, but at 15 minute intervals. These investigations were made with large bore tubes.

The fractional test meal was popularised by Ehrenreich (29) in 1912, who used a flexible narrow tube in association with an Ewald-Boas test meal, and withdrew specimens every ten minutes. The narrow bore tube was first introduced by Gross in 1893, but its value was not generally recognised until 19 years later. Rehfuss (86) gave his name to a special type of small calibre tube, and introduced it into the United States of America; Ryle (92) popularised his version in this country.

Fractional analysis made it possible to get a picture of the variation in the secretory and motor functions of the stomach during digestion. With a standard stimulus and a standardised technique, it was hoped that variations from normal would indicate pathological changes in the gastric mucosa, and give patterns of diagnostic significance, this had not

proved possible with the single aspiration method.

A disadvantage of the Ewald-Boas test meal, was the presence of solid substances during chemical analysis. In addition, during fractional analysis with a small calibre tube, there was a tendency for the solid material to block the lumen during aspiration. Thus, an entirely fluid test meal was sought. Talma, in 1895, introduced Liebeg's Extract 30%, previously neutralized with sodium hydroxide.

Boas was the first to give the oatmeal gruel test meal. Crohn and Reiss (19) 1917, used it widely, it was popularised in this country by Bennett & Ryle (4) in 1921. It was satisfactory, for not only could it stimulate the secretory activity of the stomach, but the motor function could also be studied by the presence or absence of starch in the fractional specimens.

In 1906, Kast (55) introduced alcohol, as being a pure substance and dietary in nature. Some opposed its use on the grounds that it was an irritant, and this led Katsch and Kalk (56) to propose the use of caffeine. These fluid test meals were widely used by a large number of workers, though with many variations in quantity and strength.

Garbat (37) showed that caffeine, 5% alcohol, water and an Ewald meal, each used as a stimulus to gastric secretion, gave essentially the same results; he also showed that the stomach emptied more rapidly after a fluid meal, than after an Ewald meal.

All workers reported a wide variation in

results both in healthy individuals and in those suffering from various disorders.

In 1920, Popielski (84) observed in dogs that the subcutaneous injections of histamine produced a copious gastric response. Carnot, Koskowski and Liebert (12) introduced the use of histamines in the study of human gastric activity. Rothlin and Grindlach (91) found a rough parallel between the volume of juice and the dose of histamine, and stated that histamine acted on the acid producing cells rather than on the enzyme producing ones. Histamine stimulation of gastric secretion was welcomed, as pure juice could be obtained, uncontaminated by a test meal. All investigators agreed that the gastric juice secreted in response to histamine was highly acid in character, and that a maximum response was obtained from the gastric cells.

However, Gaither (36) and also Comfort and Osterberg (16) showed that the advantages of histamine injection in place of a test meal were not sufficient to warrant the adoption of histamine stimulation as a routine. Furthermore, a stimulus given by injection instead of by the physiological route, i.e., by mouth, gave an acid secretory curve, which bore little relation to the process arising in the stomach in response to food.

The important role of histamine in the differentiation of true and false achlorhydria was established in 1925 by Gompertz and Voorhaus (41). In support of this Dietrich and Shelby (26) demon-

strated in children, and Klumpp and Bowie (58) in adults, that the acid response from histamine was greater than with any other type of stimulus; Bockhus, Bank and Willard (9) in 1932, found that only 53% of adults, in whom achlorhydria had been found after a Rehfuss test meal, failed to secrete free hydrochloric acid after histamine injection.

Footnote. Unless otherwise indicated, the material for this historical survey was extracted from references number (38) (50) (66) (77) (88).

METHODS OF GASTRIC ANALYSIS IN INFANTS

The development of knowledge of the physiology of digestion was based on work done first on animals and later on adult human beings. The study of the gastric function of children followed later, and several investigators showed that the methods evolved could be used successfully with infants and young children.

Milk is the basic diet of the infant, thus a test meal of milk would be expected to reveal the normal pattern of digestion in young children, especially those under one year of age. Milk, however, has a high buffer value due mainly to phosphates and calcium caseinate; until the buffer is saturated with acid, there cannot be an increase in the acidity of the solution. Wolman (104) found that during the first few minutes following the ingestion of milk all the free acid in the stomach is absorbed by the buffer, and the pH of the gastric contents is that of the milk itself; the pH begins to fall slowly as the digestive secretions pour out.

Human milk contains less buffer material than cows milk. Marriott and Davidson (62) showed that with the same quantities of breast and cows milk it required three times as much 0.1.N. hydrochloric acid to bring the pH to 3.4 in the case of cows milk, as compared with breast milk. They also found that in specimens withdrawn from the stomach of healthy babies 2 hours after a normal feed, the average pH

in breast fed infants was 5.3, in those fed on cows milk it was 4.75; it appeared, therefore, that in artificially fed infants, the stomach secreted a great amount of acid to counteract the stronger buffering effect of cows milk.

The milk test meal has been widely used, however, as it gives a picture of the physiological response of the stomach to normal diet. Examinations have been made sometimes after the ingestion of the infants normal feed, and, at other times, after a calculated quantity of milk, or a special milk feed. It is obvious, however, that should the hydrochloric acid secretion be low, then the presence of free acid may be masked by the buffering property of milk, which results in a large amount of combined acid.

An Ewald type of test meal is not suitable for young infants as the solid parts cannot be chewed and digested properly, and undigested lumps are thus present in the gastric contents. It has not been used in infants under one year.

Dietrich and Shelby (26) used neutral 7% ethyl alcohol as a test meal in a series of children, but all were more than 1 year of age. Steinman (99) also chose this method of gastric stimulation. Alcohol has the disadvantage of being foreign to the diet of a young infant, and also some degree of intoxication may result in a baby.

Gruel, either barley or oatmeal, was used as a test meal for children by Meyer (67) as long ago as 1898. It has been given to healthy and ill children

under 1 year by a number of workers with satisfactory results. Chievitz (14) showed in vitro that the buffering power of gruel is very low, even in comparison with an Ewald test meal. In contrasting the results obtained by using the two test meals in vivo, she showed that whereas the Ewald test meal had the greater stimulating action and gave higher figures for total acid, the gruel test meal more frequently produced larger quantities of free acid in the gastric contents, owing to its lower buffer value. In her series of 53 children under 12 months of age, using gruel, she failed to find one case with persistent achlorhydria.

It was shown in the early days of the use of histamine in gastric investigation, that there was a rough parallel between the dose of histamine and the volume of juice secreted. It is undesirable, however, to produce toxic symptoms of headache and collapse; flushing of the face and neck within five minutes of the histamine injection has been accepted as the criterion as to whether a sufficiently large dose had been given to stimulate gastric secretion. Work was done on infants and young children to determine the optimum dose. Neale (78) gave 0.15 mgm. to children under 2 years. Cutter (21) tested doses of 0.01 mgm. and .02 mgm. per kilo. in each of 9 cases; in 4 infants a higher total acidity was attained with the larger dose, in the remainder there was little difference; he noted that 0.02 mgm. per kilo. invariably produced flushing in infants.

Dietrich and Shelby (26) made a comparative study on children of methods of gastric analysis. They compared the single aspiration technique with fractional analysis, and also the results obtained by the use of Ewald and Alcohol test meals, and histamine injection. They found in children,as in adults, that fractional analysis gave higher figures for gastric acidity than the single aspiration technique, and also, that the maximum secretion of acid caused by histamine rendered it useful in distinguishing between true and false achlorhydria.

THE MEASUREMENT OF GASTRIC ACIDITY

Methods of determining gastric acidity and expressing results have varied. Gunzberg's test, introduced in 1887, was the first reliable chemical method for detecting hydrochloric acid, and in the early days specimens were examined qualitatively for the presence of free hydrochloric acid by this test and also using various indicators, such as congo red, Töpfer's Reagent, etc.

As knowledge of gastric secretion increased it was found necessary to have some method of quantitative estimation for comparing results. According to Hollander and Penner (50), Jaworski and Gluzenski introduced the system of stating the acidity in degrees in 1886. They titrated the specimen of gastric contents against 0.1 N. alkali, with litmus as an indicator, and the number of cubic centimetres of the alkali titrimetrically equivalent 100 c.c. of the specimen was taken as the number of clinical units or degrees of 0.1.N. acid present. Sodium hydroxide was quickly adapted as the standard alkali.

Töpfer's quantitative procedure has become the conventional method used in gastric analysis. Each specimen of gastric contents is titrated against 0.1.N. Sodium hydroxide using Töpfer's Reagent (dimethyl amino azo-benzol in 0.5% alcohol solution) and phenolphthalein as indicators. The results are expressed in units or degrees of free and total acid per 100 c.c. of gastric contents. The term free acid is used to denote the hydrogen ions not linked to the

buffer substance in the stomach contents and represents the amount of free hydrochloric acid present; it is measured by the number of cubic centimetres of 0.1.N. sodium hydroxide calculated to produce the first indicator colour change (i.e., the disappearance of the red colour) in 100 c.c. of gastric juice. The total acidity may be defined as the total number of cubic centimetres of 0.1.N. sodium hydroxide calculated to be required to bring the reaction of 100 c.c. of gastric juice to the end point of phenolphthalein, i.e., pH 8.3, when the red tint of phenolphthalein is at its maximum, and the second colour change has occurred during the titration.

The total acid is an index of the acid secreted by the stomach, it represents the free acid plus the entire buffer capacity. The combined acidity is the difference between the two values.

Michaelis (70) proved that a comparison of the titration curves of many gastric juices showed that all the free hydrochloric acid is just neutralized at a pH of 2.8 (salmon pink colour of Töpfer); at the yellow end point the pH is 4.5. Martin (63) demonstrated that in the pH 3 to 3.8 range, there is neutralization of much of the acid proteins and phosphate. Hollander (48) and others, have recommended the use of other indicators with an end point around pH 3.0 - 3.5 as giving a truer figure for the amount of free hydrochloric acid present.

The yellow end point of Töpfer's Reagent as an index of free acid, is in extensive use both in

present and past work.

The acidity of gastric juice is also expressed in terms of hydrogen ion concentration or pH. The strength of an acid is directly proportional to the number of free hydrogen ions present in solution, thus the action of hydrochloric acid in digestion, must be largely due to the number of hydrogen ions present. The concept of pH was introduced by Sörensen in 1909.

Work was done in the field of gastric analysis in comparing the gastric acidity determined by titration with pH estimations made by calorimetric procedure or hydrogen gas electrode. Shohl and King (96) and Christiansen (15) both reported fairly good correlation, depending on the indicator used, though this was not universally acknowledged to be true.

Since 1931, pH determinations have taken second place to titration methods, largely owing to the work of Hollander (49). He stated titration acidities gave the same information afforded by electrometric pH determinations, and were considerably more reliable for free acid values of the magnitude encountered in gastric analysis.

Modern usage is to express titration readings in normal or milli normal values - N or mN respectively. Chemical units, degrees or mN are all expressed by the same figure.

THE PRESENT INVESTIGATION

The aim of this investigation was to study the gastric function of infants under 1 year of age in health, and to find out what variation from the normal, if any, occurred in certain pathological conditions common in infancy, viz., acute primary gastro-enteritis, acute parenteral infections, pyloric stenosis, and infantile atrophy.

METHOD.

The gastric function of all the infants included in this series was examined by a fractional test meal of thin gruel. The gruel was made by adding a quart of water to two tablespoons of fine oatmeal, boiling it down slowly to one pint, and then straining it through fine gauze.

The last milk feed was given 7 hours before the test. Occasionally, water was given up to 3 hours before the start of the test meal.

A fine Ryle's Tube was lubricated with liquid paraffin and passed down into the stomach; the long end was fixed to the infant's cheek with adhesive tape. A 20 cc. Record syringe was used to withdraw the gastric contents.

The fasting juice was drawn off, and the gruel was then given via the tube in amounts equal to 1 drachm per pound of body weight. Specimens were aspirated at half hourly intervals for two hours. The free and total acidity was determined in the fasting juice, and in the four fractional samples by the Töpfer's quantitative procedure (page 14). 2 c.c.

of gastric contents were mixed with 2 to 3 drops of Töpfer's Reagent and 2 to 3 drops of phenolphthalein in a porcelain dish, and titrated with 0.1.N. sodium hydroxide, run in very slowly from a burette. ½ or 1 c.c. of gastric contents were used for titration if more was not available.

The samples were inspected for the presence of milk clots or bile. The specimen was discarded if bile was present, as this denoted dudenal regurgitation.

The emptying time of the stomach was estimated by the addition of a few drops of iodine solution to each specimen, the presence of starch being shown by an intense blue coloration.

The figures treated as significant in the thirty minute samples have been maximum free acidity and maximum total acidity.

In some cases showing an absence of free acid in all specimens, the gruel test meal was repeated within 48 hours, with the addition that histamine (ergamine acid phosphate - Burroughs Welcome) was injected subcutaneously, immediately the gruel had been introduced through the Ryle's tube. The dose of histamine used was 0.02 mgm. per kilo. of body weight.

Further investigations were made in some infants. The fractional test meal of gruel was repeated later in the disease, or during convalescence, or recovery. On occasions the gruel meal was also given again when the infant was readmitted during a relapse or with a different disease.

NORMAL INFANTS.

An investigation into the influence of disease on gastric function, must be preceded by a study of the gastric function of healthy infants to obtain standards for comparison.

Some of the earliest work in this field was done on newborn babies. Hess (45) aspirated the gastric contents of 52 infants less than 18 hours old, he found free hydrochloric acid in all but one case. The fasting volume varied greatly, exceptionally one infant gave 10. c. c. and another 12 c. c., but the majority gave between 0.25 and 5.0 c. c. Acid was obtained throughout a prolonged period, in spite of the absence of food, thus indicating a continual secretion; in one case, 17 c. c. of highly acid juice was secured in 1 hour 50 minutes, with free acid ranging between 30 and 56 units. From comparative tests in some of the same infants a few days later, he concluded that the stimulus to gastric secretion was probably greater in the newborn.

Pollitzer (83) made similar observations on 100 unfed newborn babies; he found individual variations in the amount and concentration of free hydrochloric acid, but no cases of achlorhydria.

In contrast, Banu, Heresce and Negresco (2) did not find any free hydrochloric acid in the gastric contents of the newborn until the sixth day of life.

Griswold and Shohl (42) in their series of 25 unfed newborn infants found an average pH of

2.6 (range pH 1.7 - 4.4). They examined the gastric contents on the 5th and 10th days of life, 1 hour after a test meal of milk; the average pH on both occasions was about the same as at birth, but the range of variation was narrower (pH 2.0 - 3.0) They considered that gastric digestion was greater in the newborn than later in infancy, as 76% of the children aged 3 - 19 months, whom they tested, gave a range of pH 3.9 - 4.6 in the gastric contents.

Ritter (87) in a more recent paper investigated 36 infants ½ - 14 hours old, and unfed. He found the fasting free acid ranged from 0 - 56 units, and the fasting total acid from 11 - 84 units. There was no free acid in the gastric contents of 4, though more than 50% gave free acid values of over 20 units, reaching 56 units in one instance. The pH range was 1.28 - 4.59, somewhat wider than Griswold and Shohl's figures.

These high values in the immediate post-natal period were systematically investigated by Miller (71), who followed the fasting juice of 50 normal infants from birth to 4 weeks of age. He found a steady decline of gastric acidity during the first ten days of life, thereafter there was a very gradual rise. He considered that the maximum acidity was reached within 24 - 48 hours of birth, the average of the highest reading for each infant during the first 48 hours was 21.6 c.c. 0.1 N free acid and 45.9 c.c. 0.1 N. total acid. On the tenth day, these figures had fallen to 0.0cc. and

11.7 c.c. respectively. 12% of the infants showed an absence of free acid in the fasting juice throughout the 4 week period. The volume of fasting juice secreted was directly related to the acidity, and the lower the fasting acidity, the poorer the response of the gastric mucosa to the stimulus of a test meal of milk.

In a series of infants, aged 0 - 12 months, to whom Miller (72) gave a fractional test meal of milk, he found free acid almost always absent in the test meal specimens, from the latter half of the first week to the middle of the third week of life; thereafter, increasingly fewer babies showed achlorhydria, until at 12 weeks of age, 76% of the infants showed free acid during the test meal. A steady rise in total acidity from the third week was noted. Examinations at 24 weeks and 1 year showed a tendency for the concentration of acid to rise.

Cutter (21) employed histamine stimulation of gastric secretion in 72 infants, 4 days to 4 years old, 50 of his subjects were under 1 year of age. The infants over 10 days old were almost without exception convalescent from various disorders, including respiratory infections, eczema, diarrhoea, acute otitis media; none were febrile. His results are summarised in Table I. Two children aged 20 and 22 days failed to secrete any gastric juice, so have been omitted from this Table, thus leaving 48 infants under 1 year of age.

Table I. Gastric acidity after histamine stimulation (Cutter)

Age in weeks.	Number of infants.	Free acid mN.	Total acid mN.	Combined acid mN.
0-2	9	8.67	27.22	18.55
3-4	4	1.00	10.43	9.43
5-12	8	17.45	31.06	13.61
13-26	9	23.33	39.18	15.85
27-39	12	27.25	41.70	14.45
40-52	6	44.73	64.48	29.75

His findings as to the trend of gastric secretion correspond with those of Miller (72), they will be discussed more fully later.

It was considered by the earlier workers that there was little or no rise in gastric acidity during the first year of life. Most of the opinions were based on pH determinations made on gastric contents obtained by the single aspiration technique. Specimens were removed at varying times after normal feeds, or after specially prepared milk feeds.

Hahn (43) examined 91 specimens from 37 children under 1 year of age, withdrawn from the stomach 1 hour after a milk feed. He concluded there was very little change in the pH of gastric contents in the first 12 months of life, but if his figures are examined carefully it is found that there is a progressive fall in the pH from 5.2 in the first month to 4.5 in the fourth trimester.

Davidsohn (22) was unable to show that age increased the gastric acidity except in breast fed infants. Under 7 months, the pH had a range of 3.62 - 6.2, the actual figure being influenced

largely by the dilution and the type of milk. He thought that the pH of the gastric contents of breast fed infants rose sharply to an average of 2.92 from 7 months to 1 year, due to the progressive development of the acid secreting power of the stomach. The rise in the acidity in the stomach of artificially fed infants was masked by the greater buffering qualities of the milk, though cow's milk was less stimulating to gastric secretion than breast milk.

Marriott and Davidson (62) also recognised this variable buffer action of milk. They found the average pH of the gastric contents of 41 normal breast fed infants under 1 year to be 3.75. In a comparable group of infants, artificially fed the pH was 4.75. If breast fed infants were given a feed of cow's milk, the average pH of the gastric contents at the height of digestion was 5.3.

Babbott et al (1) using a test meal of cows milk made 55 observations on 31 convalescent infants. The average pH of 4.6 in the 2 - 9 months group compared with a pH of 4.2 in the 12 - 19 months group, led them to conclude that acid production increased slightly with age.

Wills and Paterson (103), on the other hand, were not convinced that age influenced results. They removed the stomach contents after an ordinary feed by the fractional method or by a single aspiration. Associated with the use of the fractional method of gastric analysis, they found lower pH figures than previous workers, the average maximum pH being 3.02

for normal infants aged 1 - 9 months whether breast or artificially fed. They agreed with other investigators that wholly breast fed babies had a higher gastric acidity. Klumpp and Neale's work (59) also did not reveal any upward trend in the first year.

Gruel test meals were first used in the study of gastric acidity in infants by Meyer (67). Hertz (44) adopted this method also. Chievitz (14) gave gruel test meals to a small series of 10 normal infants under 1 year of age. She aspirated the whole of the stomach contents after 35 to 45 minutes. The gastric acidity in the group was lower than in older children or adults. If her results are studied more closely, it is found that in the 8 artificially fed children, aged 3 to 11 months, there was a tendency for the free and especially the total acidity to increase with age. In the case of 2 breast fed children, both 2 months old, the free and total acid was as high as the amount found at 7 - 9 months in the artificially fed group, this agrees with Marriott and Davidson (62) and Wills and Paterson (103) mentioned above.

Müller and Gutschmidt (76), using the same technique, widened and extended Chievitz's work (14). They believed that free and total acid was low during the first 3 months of life but thereafter increased with age. Following up 3 cases under 3 months of age they noted that there was achlorhydria at first, but from 10 weeks of age free acid was found

during the test meal.

A thin wheat flour gruel was given to 36 infants by Izumita (53). He considered that the buffer value of this fluid was less than gruel. A summary of his findings has been made and is given in Table II.

Table II. Gastric Acidity after wheaten gruel (Izumita)

Age in months.	Number of infants.	Free Acid mN.	Total Acid mN.	Combined Acid mN.
1-3	12	5.00	10.83	5.83
4-6	8	6.25	11.88	5.63
7-9	9	5.0	11.55	6.55
10-12	7	8.28	15.14	6.86

The values for free, total and combined acid are all low. There is slight increase of acidity with age.

PRESENT INVESTIGATION.

The gastric function of 24 normal babies under 1 year of age was investigated by giving each a fractional test meal of gruel. Nineteen of these infants were in the nurseries attached to the Maternity Wards of the Glasgow Municipal Hospitals, they were all healthy and had no history of illness. The remaining 5 were admitted to the wards of the Royal Hospital for Sick Children, Glasgow; they were at no time acutely ill, had no gastro-intestinal upset, and were being investigated for such conditions as paroxysmal tachycardia, oxycephaly, hydrocephalus due to birth injury, etc.

The results are given in Appendix A, and are summarised in Table III.

Table III. Gastric Acidity. Normal Infants.

Name	Age in wks.	Fasting juice		Fractional Test Meal		
		Free Acid mN	Total Acid mN	Free Acid mN.	Total Acid mN.	Combined Acid mN.
1. G. C.	3	0	A	0	10.2	10.2
2. C. B.	3	0	6.0	4.0	21.5	17.5
3. -. R.	3½	1.0	8.0	1.5	17.0	15.5
4. A. T.	3½	5.0	9.0	3.0	8.0	5.0
5. D. B.	6	+	A	5.0	44.0	39.0
6. F. R.	7	5.5	11.0	22.0	36.0	14.0
7. B. F.	7	0	A	21.0	36.0	15.0
8. A. W.	9	5.0	13.0	18.0	20.0	2.0
9. -. B.	9	0	A	4.0	22.0	18.0
10. -. M.	11	16.0	44.0	13.5	32.5	19.0
11. A. W.	12	2.0	8.0	4.0	38.0	34.0
12. -M.	12	8.0	28.0	15.5	35.5	20.0
13. -. B.	13	0	A	8.0	30.2	22.2
14. R. W.	16	10.0	30.0	19.5	42.0	22.5
15. -. H.	18	2.0	9.5	14.8	34.5	19.7
16. A. T.	20	0	36.0	14.0	29.0	15.0
17. A. H.	22	5.0	18.0	16.0	33.0	17.0
18. M. B.	28	0	10.0	13.2	25.5	12.3
19. -. W.	28	0	28.0	19.0	36.0	17.0
20. -. A.	35	+	A	18.5	32.0	13.5
21. B. G.	40	12.0	32.0	19.0	33.0	14.0
22. -. M.	42	+	A	17.4	28.0	10.6
23. -. R.	45	6.4	20.0	20.0	40.0	20.0
24. A. B.	48	2.0	6.0	23.0	50.0	27.0

\+ = free hydrochloric acid, qualitative test with Töpfer's Reagent.
A = amount of gastric contents sufficient only for qualitative test for free hydrochloric acid.

The date was divided into age groups and the average acidity for each group calculated, the general trend of gastric secretion during the first year of life was made clearer (Table IV. Graph I). The age groups have been chosen in view of the trend of the findings of Cutter (21) and Miller (72).

Table IV. Gastric Acidity. Average in age groups.

Age in weeks	No. of infants	Fractional test meal		
		Free Acid mN.	Total Acid mN.	Combined Acid mN.
3-4	4	2.13± 1.06	14.18 ± 2.68	12.05
5-12	8	12.88± 2.50	33.00 ± 2.68	20.12
13-26	5	14.46± 1.67	33.74 ± 2.30	19.28
27-39	3	16.90± 1.51	31.17 ± 2.48	14.27
40-52	4	19.85± 1.02	37.75 ± 4.13	17.90

The secretion of free acid was low at 3 to 4 weeks, being 2.1 mN (range 0.0 - 4.0). There was a sharp increase between 5 and 12 weeks to 12.9 mN (range 4.0 - 22.0). From 13 weeks to 1 year the rise was slow being only 7 mN compared with the rise of 10.8 mN between the 3 to 4, and 5 to 12 week periods. At 13 to 26 weeks the free acid was 14.5 mN (range 8.0 - 19.5), at 27 to 39 weeks it was 16.9 mN (range 13.2 - 18.5) and at 40 to 52 weeks, 19.9 mN (range 17.4 - 23.0).

Only 1 case of achlorhydria was noted, this was in an infant 3 weeks old, the lowest age examined. Coincident with this, as age increased, the minimum amount of free acid present, reached a progressively higher figure in each age group.

The total acidity ran roughly parallel to the free acidity, but at a higher level. It was low at 3 to 4 weeks, being 14.2 mN (range 8.0 - 21.5). The rise in the 5 to 12 week period was even more acute than in the case of the free acid, a value of 33.0 mN (range 20.0 - 44.0) was reached giving an increase of 18.8 mN, contrasted with a very small rise to 37.8 mN (range 28 - 50) at 39 to 52 weeks.

The combined acidity was 12.1 mN (range 5.0 - 17.5) in the 3 to 4 weeks period, its lowest value. There was a sharp rise at 5 to 12 weeks, to a figure which remained almost the same in the second trimester. During the last 6 months of the first year, there appeared to be a tendency for the combined acid to decrease slightly.

A wide variation in the gastric acidity of healthy infants was apparent.

Time of Maximum Secretion of free acid.

Throughout this investigation, in each individual case, the time of maximum secretion of free acid was taken as the time at which the specimen containing the maximum amount of free acid was aspirated during the fractional test meal.

The majority of infants produced a maximum secretion of free hydrochloric acid within 1 hour of receiving the test meal stimulus. (Table V).

Table V. Time of maximum secretion of free acid during test meal.

Time of maximum secretion of free acid.	Number of infants.	% of total infants having free acid during test meal.
½ hour specimen	6	26.1
1 hour specimen	14	60.9
1½ hours specimen	2	8.7
2 hours specimen	1	4.3

From these figures a Percentile Curve was drawn (Graph II); from this it was found that the median time was 43½ minutes, i.e. the time when 50% of the infants have had their maximum secretion; the interquartile range was 28½ to 55½ minutes. A fair estimate of the time of maximum secretion for this group was thus 43½ ± 13½ minutes. In other words, 50% of the group had their maximum secretion of free acid between 30 and 57 minutes after the test meal stimulus was given, and there was an equal probability of any one individual having their maximum secretion before or after 43½ minutes (see Appendix F).

The Emptying Time of the Stomach.

No gastric contents were withdrawn more than two hours after the gruel was given, throughout the entire series.

The stomach took over two hours to empty in 66.7% or two-thirds of all the infants. In 20.8% the time required was 1½ to 2 hours, and in 12.5% it was 1 to 1½ hours.

Table VI. Emptying Time of Stomach.

Emptying time in hours.	Number of infants.	% of total infants.	Aver. free acid mN.	Aver. total acid mN.
Over 2	16	66.7	14.8	31.96
1½ - 2	5	20.8	9.4	30.8
1 - 1½	3	12.5	10.2	23.2
½ - 1	0	0	0	0
0 - ½	0	0	0	0

Over the age of 12 weeks, 11 of the 12 infants gave an emptying time of over 2 hours whereas under 3 months this time was required by only 5 out of 12. In 5 out of the 7 infants under 8 weeks of age, the emptying time was under 2 hours. It would appear, therefore, that the stomach empties more rapidly in young babies than in older ones. It may be argued, that the older infants were heavier and this received more gruel initially, but it must also be remembered that in everyday life an older child is heavier and thus receives a larger feed than a younger one.

Neglecting the age, the average acidity was worked out for each emptying time. The free and total acid was highest in those infants with the longest emptying time.

Fasting Juice.

In nearly one third of all the infants, the fasting juice was so small in amount, that only a qualitative test for hydrochloric acid was done. Amounts up to 4 c.c. were withdrawn in the other cases.

Eight infants had no free acid in the fasting juice, all but 1 of these secreted hydrochloric acid in response to the gruel stimulus. When free acid was present in the fasting juice, it was also found during the fractional test meal. Two infants showed a higher value for free and total acid in the fasting juice than during the test meal.

Comments.

It has been shown in this investigation that the secretory power of the gastric mucosa increases during the first year of life.

The gastric acidity is low in the 3 to 4 week period. There is a rapid rise between 1 and 3 months, followed by a much slower rate of increase thereafter. The rate of increase of the total acidity between 1 and 3 months is more rapid than that of the free acidity. There is a tendency to a decrease in the combined acidity during the second 6 months of life.

The increasing gastric function is also shown by the fact that the only case of achlorhydria in the series was in the youngest age group, when the secretion of free acid was lowest. As age advances, there is a rising minimum figure for free

hydrochloric (and total) acid. Ihre (51) stated that in adults, the degree of acidity varied directly as the rate of secretion; this was confirmed in infants by Miller (72).

Oatmeal gruel is a much stronger stimulus to gastric secretion in infants than Izumita's wheat flour fluid (53).

Bennett and Ryle (4) in their investigation of 100 healthy adults using a fractional test meal of gruel, found that the mean maximum percentage of free acid was 33% 0.1 N hydrochloric acid. The total acidity followed a curve of concentration parallel to the free acidity, and was 10% higher, giving a mean maximum of 43% 0.1 N acid. In this series, it is seen that at 1 year, the gastric secretory function has not yet reached adult level, and the combined acidity is greater.

Histamine produces a maximum acid concentration in the individual. In Cutter's (21) series of normal infants to whom he gave histamine, we find in the 37 to 52 weeks age period, an average free acid of 44.73 mN and average total acid of 64.48 mN. This represents pure gastric juice, undiluted by a test meal, and is the greatest effort the gastric mucosa can make at this age. Achlorhydria was found in 3 of the 4 infants in the 3 to 4 weeks old group in the histamine series, and in 1 of 4 infants in the present investigation using a test meal of gruel.

Comparing the results obtained with histamine and with gruel it is found that the curves for the free and total acid have the same pattern (Graph III a and b). Using histamine, the gastric acidity is low at 3 to 4 weeks; there is the same sharp rise in the 5 to 12 week period as with gruel, followed by a more gradual rise up to 1 year. The rate of increase of the acidity is more rapid with histamine than with gruel, and the free and total acidity at 40 to 52 weeks reaches a considerably high level. The results with histamine show the same large rise in combined acids in the 5 to 12 week period, a tendency to a fall in the 27 to 39 week period, and a rising amount again in the last quarter of the year.

The results, using a fractional test meal of gruel to study the gastric acidity in infants under 1 year, compare satisfactorily with those obtained by the maximum stimulation of histamine. The overall physiological pattern is similar, though the figures for the free and total acidity using histamine are higher, especially after three months of age.

Miller's use of a cow's milk test meal (72) in his study of infants under 1 year of age must largely explain the large number of achlorhydric infants found by him. At the end of the third week of life, free acid was present in 50% of the test meals, yet by 12 weeks this figure had only reached 76%. Though milk is the physiological diet of the baby, a test meal of milk is not the best

method of investigating gastric acidity, for the infants with low hydrochloric acid secretion may show achlorhydria due to the potent buffers in the milk absorbing the free acid. A gruel test meal is superior to milk.

The fasting juice is not a reliable index of the acid secreting power of the stomach. In the 23 cases that secreted free acid during the test meal, 7 of them failed to show free acid in the fasting juice. This agrees with Miller's findings (72) in the majority of infants after the third week of life.

Parsons (81) stated that the average emptying time of the stomach in infants is 2 to $2\frac{1}{2}$ hours. Miller (72) showed that over 50% of babies in his series required more than 3 hours.

Willox (102) studied a series of children using x-rays and found that the stomach of older children emptied as quickly as that of younger ones, if a meal of similar bulk and consistency is given, the more fluid the meal the quicker the emptying. He gave the average time as $3\frac{3}{4}$ hours, the youngest child, however, was 17 months old.

Ogilvie (79) took all the children in her series together, they were 0 - 12 years old. She noted that in 63%, the stomach was empty at 2 hours. She used a fractional test meal of gruel, as did Bennett and Ryle (4) who demonstrated that the average emptying time of the stomach in adults was 1.9 hours.

In the present investigation, the majority of infants had an emptying time of over 2 hours.

Miller (72) considered that the stomach emptied more rapidly as the infant grows older, this is opposite to the findings here.

Morse (74) experimented on dogs, and showed that the rate of discharge of fluid from the stomach decreased with increase of acidity. Cowie and Lyon (18) carried out a series of tests in infants, by placing solutions of a different pH in the stomach; they found that the emptying time was prolonged when there was an excess or a deficiency of acid.

According to Davidsohn (22) the mobility of the stomach in childhood varied directly with the gastric acidity. Babbot et al (1) found the higher the acidity the more rapid the emptying, and Marriott and Davidson (62) observed that in infants with deficient gastric acidity a larger amount of fluid could be recovered 2 hours after a test meal, than in other infants.

In this series, the highest figures for free and total acid were present in those infants with an emptying time of over 2 hours. This agrees with the work of Morse (74) in dogs, but is opposite to the results of the other workers just mentioned.

<u>Summary.</u>

In a study of gastric function in normal infants under 1 year of age, the following conclusions were reached.

(1) a fractional test meal of gruel is a

satisfactory method of gastric analysis.

(2) Gastric acidity increases during the first year of life, the rise is especially rapid in the 5 to 12 week period.

(3) The combined acidity increases rapidly at 5 to 12 weeks. It tends to decrease in the second 6 months of life.

(4) The acid secreting power of the gastric mucosa increases with age, as shown by the rising minimum figures for free and total acidity in the successive age periods.

(5) 1 case of achlorhydria was noted out of 24 infants examined; this occurred at 3 weeks.

(6) The fasting juice is not a reliable index of gastric secretion.

(7) The estimated time of maximum secretion of free hydrochloric acid during a fractional test meal of gruel is $43\frac{1}{2} \pm 13\frac{1}{2}$ minutes.

ACUTE PRIMARY GASTRO-ENTERITIS.

The term acute primary gastro-enteritis is used for the cases of diarrhoea and vomiting associated with profound constitutional upset, which remain after excluding other causes of this clinical picture, viz. (a) the specific gastro-intestinal infections, e.g., dysentery and typhoid, (b) local causes of diarrhoea such as pelvic appendicitis and peritonitis, (c) diarrhoea symptomatic of general disease, (d) digestive disorders.

Observations on the gastric function of infants under 1 year of age suffering from acute primary gastro-enteritis have been few.

Chievetz (14) included only 1 case in her series of 26 infants under 1 year of age, suffering from digestive disturbances. A gruel test meal was given three times in the course of the infection, the total acidity was low on all occasions, a small quantity of free hydrochloric acid was present on the first examination, but none was found subsequently.

Davison (23) noted that in digestive disturbances in infants, especially in diarrhoea, there was reduced acidity in the duodenal contents. Practically no difference was found in the reaction of the gastric contents of normal infants, and those convalescent from diarrhoea.

More work has been done in older children, which may be mentioned, though this present investigation is confined to infants less than 1 year old. Jacobsen (54) investigated 6 children

aged 14 months to 3 years, in the acute stage of gastro-enteritis, using an Ewald test meal. He found a reduced hydrochloric acid secretion in 5; one of these he followed up and found that the secretion increased, as the child improved. In sub-acute and chronic gastro-enteritis, three quarters of the children showed hypo or achlorhydria, there was a marked improvement in the secretion of hydrochloric acid, as the condition cleared up. Klementsson (57) examined children aged 1 to 12 years, also using an Ewald test meal, his findings agreed with Jacobsen (54).

The influence of a raised temperature per se on gastric secretion has been demonstrated on human beings and on animals. Meyer et al (69) in a series of experiments performed on dogs, found that during fever, the gastric secretion after food was diminished in volume, and in free and total acidity. An injection of gastrin was unable to stimulate a secretion of gastric juice. These changes were present during the febrile period only, next morning the gastric secretion was normal.

Ylppö (105) in some experimental observations on young infants, found that whether a rise in temperature was induced by infective or mechanical means, the mean hydrogen ion concentration of the gastric juice was about 1 point higher on the pH scale, than before the induction of the artificial fever. The majority, but not all, of these infants showed this reduction in gastric acidity.

Davison (23) (24) discussed the influence of a raised temperature on the gastric acidity of ill children. He noted a reduced acidity in slightly febrile infants, convalescent from diarrhoea, and cited Marriott and Davidson's findings (62) of lowered gastric acidity in children with acute and chronic infections who had almost certainly been febrile. He concluded that it was probable that fever was largely responsible for the reduction in gastric acidity, but that the production and swallowing of a large amount of saliva by these children might be an important factor.

Observations in acutely ill adults were made by Chang (13). He studied gastric secretion by the histamine method in 106 febrile adults. He found an average decrease of gastric acidity to a third of the normal, with a similar though less marked change in the volume of the secretion. The decrease of gastric function was considered to be proportional to the height of the fever. Recovery occurred in convalescence.

PRESENT INVESTIGATION.

In the present investigation, the gastric function of 51 infants under 1 year of age, suffering from acute primary gastro-enteritis (in future the word primary will be omitted) was examined using a fractional test meal of gruel. In view of the fact that these infants were acutely ill, it was deemed inadvisable to submit them to 7 hours complete fast, thus although the last feed was given 7 hours

Table VII. Gastric Analysis - Acute Gastro-enteritis.

Name.	Age in wks.	Fasting Juice. Free Acid mN.	Fasting Juice. Total Acid mN.	Fractional Test Meal. Free Acid mN.	Fractional Test Meal. Total Acid mN.	Fractional Test Meal. Combined Acid mN.
1. E. D.	3	0	75.0	0	23.0	23.0
2. S. D.	4	0	21.0	0	28.0	28.0
3. M. H.	5	0	A	0	47.0	47.0
4. J. S.	5	0	A	0	36.0	36.0
5. S. B.	6	4.0	57.0	14.0	38.0	24.0
6. P. F.	6	0	15.0	3.0	20.0	17.0
7. J. G.	6	0	43.5	9.5	28.5	19.0
8. C. H.	6	0	17.0	0	66.0	66.0
9. W. J.	7	0	A	0	16.0	16.0
10. I. R.	8	/	/	20.5	45.0	24.5
11. J. M.	8	0	30.0	17.0	39.0	22.0
12. T. G.	9	0	37.4	0	23.0	23.0
13. A. B.	9	0	13.0	0	19.5	19.5
14. C. C.	10	0	33.0	0	18.0	18.0
15. N. G.	10	0	10.5	33.0	51.0	18.0
16. T. C.	11	0	20.0	40.0	72.0	32.0
17. M. K.	12	0	32.5	39.0	61.0	22. 0
18. C. K.	12	0	A	6.0	25.0	19.0
19. S. C.	13	0	25.0	5.0	22.0	17.0
20. M. C.	13	0	33.0	0	12.0	12.0
21. C. L.	15	0	12.0	0	12.0	12.0
22. H. F.	16	0	A	0	46.0	46.0
23. M. G.	16	0	20.5	7.5	19.0	11.5
24. R. P.	16	0	22.0	48.0	89.0	41.0
25. M. R.	16	0	8.0	0	37.0	37.0
26. D. S.	16	/	/	25.5	54.0	28.5
27. L. D.	17	0	A	0	39.0	39.0
28. J. C.	17	0	14.5	0	42.0	42.0
29. M. G.	18	0	38.0	0	79.0	79.0
30. A. S.	18	0	82.0	0	81.0	81.0
31. H. G.	18	0	22.0	0	22.0	22.0
32. M. M.	19	0	31.0	3.0	39.0	36.0
33. R. R.	19	0	36.5	0	41.0	41.0
34. P. K.	21	0	35.0	6.0	29.0	23.0
35. D. D.	21	0	26.0	0	39.0	39.0
36. R. L.	22	0	A	0	10.0	10.0
37. E. K.	23	0	8.0	8.0	29.0	21.0
38. I. N.	23	22.0	52.0	26.5	42.5	16.0
39. J. H.	26	0	A	0	7.0	7.0
40. F. H.	26	0	20.5	10.0	24.0	14.0
41. H. M.	26	0	A	0	70.0	70.0
42. A. M.	26	0	A	0	32.0	32.0
43. R. M.	27	0	17.0	10.5	46.0	35.5
44. E. L.	28	0	A	7.0	28.0	21.0
45. J. F.	32	0	32.0	0	45.0	45.0
46. J. S.	34	0	20.0	0	24.0	24.0
47. A. S.	34	0	24.5	0	30.0	30.0
48. H. M.	36	0	47.0	0	17.0	17.0
49. A. S.	44	0	10.0	0	22.0	22.0
50. M. T.	48	0	22.0	0	25.0	25.0
51. J. B.	49	0	A	0	45.0	45.0

+ = free hydrochloric acid qualitative test with Töpfer's Reagent.

A = amount of gastric contents sufficient only for qualitative test for free hydrochloric acid.

/ = stomach empty.

Table VIII. Gastric Acidity, Average in Age groups. Acute gastro-enteritis.

Age in wks.	No. of infants.	No. with achlor-hydria.	Fractional test meal. Free Acid mN.	Total Acid mN.	Comb'd. Acid mN
3-4	2	2	0	25.50±1.77	25.50
5-12	16	7	11.38±3.53	37.84±4.34	26.46
13-26	24	15	5.81±2.33	38.19±4.54	32.38
27-39	6	4	2.92±1.73	31.67±4.32	28.75
40-52	3	3	0	30.67±5.89	30.67

before the test meal was started, water ad. lib. was offered up to 3 hours before the gruel was given.

The results are given in Appendix B., and are summarised in Table VII.

The infants were divided into the same age groups as the normal children and the results in each group averaged, so that the data could be compared (Table VIII and Graph IV).

In acute gastro-enteritis, 61% of the infants had achlorhydria. The average value for free acid was lower than normal in all age groups. The depression below the normal figure was increasingly marked as age increased; at 5-12 weeks the difference was 1.50 mN, but at 3-6 months it was 8.65 mN., at 6-9 months, 13.98 mN and at 9-12 months it had reached 19.85 mN.

The total acidity showed little change from the findings in normal children, but the combined acidity was noticeably increased in all age groups.

The infants were graded into 3 groups according to the severity of the infection - severely, moderately and mildly ill. The grading was assessed clinically on the degree of toxaemia and dehydration present. The severely ill were dehydrated, limp, pale and toxic, 5 of these subsequently died; the moderately ill group showed slight dehydration and moderate toxaemia, whilst the mild cases were not dehydrated and showed only mild toxaemia.

Table IX. Severity of Illness and Achlorhydria.

Grade of illness.	Number of infants.	Infants with achlorhydria.	
		Number.	% in group.
Severe	19	15	78.9
Moderate	16	10	62.5
Mild	16	6	37.5

The incidence of achlorhydria increased with the severity of the illness. In severe infections nearly four-fifths of the infants failed to secrete free hydrochloric acid during the fractional test meal, this was more than twice the figures for those who were mildly ill.

The free and total acidity of these infants with a temperature elevation to 100°F. or over during the 24 hours before the test meal, was compared with the values for those free from fever, but no consistent variation was noted. However, it must be mentioned that all the infants had shown fever at some time in the

course of the illness before their gastric function was investigated.

Time of maximum secretion of free acid.

In acute gastro-enteritis, Table X shows that the time of maximum secretion of free acid during the gruel test meal was later than in normal children. This was further brought out by the Percentile Curve.

Table X. Time of maximum secretion of free acid during test meal.

Time of maximum secretion of free acid.	Number of infants.	% of total infants having free acid during test meal.
½ hour specimen	2	10
1 hour specimen	6	30
1½ hours specimen	5	25
2 hours specimen	7	35

From Graph V it was found that the median time was 72 minutes, and the interquartile range was 45 - 99 minutes. It can be estimated that the time of maximum secretion was 72 ± 27 minutes, thus 50% of the children who secreted free acid had their maximum secretion between 45 and 99 minutes after the test meal stimulus was given.

Compared with normal infants, the median time was considerably later (28½ minutes); the estimated time of maximum secretion started later and was more prolonged being double that of normal.

The Emptying Time of the Stomach.

In acute gastro-enteritis there was a tendency for the stomach to empty more rapidly than in normal infants (Table XI).

Table XI. Emptying Time of Stomach.

Emptying time in hours.	Number of infants.	% of total infants.
Over 2	30	58.8
$1\frac{1}{2}$ - 2	12	23.5
1 - $1\frac{1}{2}$	8	15.7
$\frac{1}{2}$ - 1	1	2.0
0 - $\frac{1}{2}$	0	0

58.8% of the infants with acute gastro-enteritis still gave a positive Starch/Iodine reaction at 3 hours, compared with 66.7% in normal infants, a difference of nearly 8%.

Fasting Juice.

It was possible to aspirate a varying quantity of fasting juice from the stomach of all but 2 of the 51 infants, though in 11 the amount was so small (under $\frac{1}{2}$ c.c.) that a quantitative estimation of acidity was not made. Free acid was present in only 2 of the 49 specimens obtained, the quantity of free acid was smaller than during the fractional test meal. The total acid was as high or higher in the fasting juice than during the test meal in 14 instances.

RE-EXAMINATIONS WITH COMBINED GRUEL AND HISTAMINE STIMULUS.

It was noted that 31 of the 51 infants (or 61%) suffering from acute gastro-enteritis, had no free hydrochloric acid in the gastric contents during the fractional test meal or when fasting.

Eighteen of the 31 infants with achlorhydria were re-examined within 2 days of the first estimation, a fractional test meal of gruel was given combined with a subcutaneous injection of histamine. The results are given in Appendix B, and are summarised in Table XII.

Table XII. Gastric Acidity with combined gruel and histamine stimulus.

Name.	Fractional test meal.		
	Free Acid mN.	Total Acid mN.	Combined Acid mN.
1. E. D.	6.5	28.0	21.5
4. J. S.	4.0	71.0	67.0
8. C. H.	6.0	66.0	60.0
12. T. G.	10.0	44.0	34.0
13. A. B.	3.0	20.5	17.5
14. C. C.	11.0	55.0	44.0
20. M. C.	7.0	45.0	38.0
21. C. L.	0	14.0	14.0
22. H. F.	5.0	28.6	23.6
29. M. G.	14.0	39.0	25.0
30. A. S.	5.0	81.0	76.0
31. H. G.	7.0	33.0	26.0
33. R. R.	20.5	55.0	34.5
39. J. H.	0	6.0	6.0
41. H. M.	10.0	31.0	21.0
42. A. M.	5.5	52.0	46.5
49. A. S.	12.0	20.0	8.0
50. M. T.	0	23.0	23.0

With the combined gruel and histamine stimulus, it was found that only 3 of the 18 infants showed lack of hydrochloric acid in the gastric secretion. As these 18 infants were chosen by random selection, the results may be applied to the whole series, thus it can be calculated that of the 51 infants, 10.1% would show no acid even with the strong stimulus of histamine combined with gruel.

The amount of free acid secreted was low compared with the range for normal infants using gruel alone. The 3 infants with persistent achlorhydria showed very little alteration in the figure for total acidity, thus indicating that no hydrochloric acid had been secreted and had been neutralised by buffer substances. Twelve of the 15 other infants showed total acid figures equal to or greater than those found in the initial test meal.

RE-EXAMINATIONS DURING RELAPSE.

Two infants were examined again using a fractional test meal of gruel, when they were re-admitted during a relapse. (Table XIII and Appendix B).

Table XIII. Gruel test meal repeated during Relapse.

Name.	Intervals after 1st. test meal.	Fractional test meal.		
		Free Acid mN.	Total Acid mN.	Combined Acid mN.
12.T.G.	17 days	0	54.0	54.0
14.C.C.	20 days	0	28.0	28.0

Both showed achlorhydria at the initial examination and during the relapse. They had both secreted free hydrochloric acid in response to the combined gruel and histamine stimulus.

Neither survived their second period in hospital.

RE-EXAMINATIONS DURING CONVALESCENCE AND RECOVERY.

It was desired to follow up some of the group of 51 infants and to demonstrate any change in the gastric secretion during and after convalescence, this was done in 14 cases, who were all now free from gastro-intestinal symptoms. Each was given a fractional test meal of gruel and the results compared with the first examination during the acute stage of the disease.

The majority of the babies reported for the examination as out-patients. In two instances, Nos. 42 and 43, the babies were still in hospital, though No. 42 was investigated again later when an out-patient.

Table XIV. Gruel test meal repeated during Convalescence.

Name.	Interval after 1st. test meal in days.	Fasting Juice. Free Acid mN.	Fasting Juice. Total Acid mN.	Fractional test meal. Free Acid mN.	Fractional test meal. Total Acid mN.	Fractional test meal. Comb'd. Acid mN.
1. E.D.	27	0	44.0	8.0	50.0	42.0
2. S.D.	21	0	13.0	14.0	61.5	47.5
15. N.G.	55	25.0	62.0	0	46.0	46.0
17. M.K.	59	7.0	69.0	0	84.0	84.0
21. C.L.	45.	28.0	88.0	0	31.0	31.0
26. D.S.	26	12.5	44.5	15.0	55.0	40.0
28. J.C.	25	21.0	58.0	3.0	35.0	32.0
32. M.M.	26	0	44.0	9.0	28.0	19.0
36. R.L.	36	4.0	14.0	5.0	35.0	30.0
41. H.M.	32	0	125.0	32.0	63.0	31.0
42. A.M.	8	0	69.0	2.0	34.0	32.0
42. A.M.	32	/	/	11.0	66.0	55.0
43. R.M.	8	/	/	28.0	81.0	53.0
44. E.L.	51	0	8.0	12.0	83.0	71.0
48. H.M.	36	7.0	56.0	0	37.0	37.0

(/ = stomach empty)

When acutely ill, 8 of these 14 infants had shown achlorhydria. During convalescence and recovery all the infants showed free hydrochloric acid in the gastric contents, either in the fasting juice or during the fractional test meal, the secretion having returned after as short an interval as 8 days. (Table XIV. and Appendix B). The amount of free hydrochloric acid increased as convalescence advanced. (No. 42)

It was noted that 4 cases showed a secretion of hydrochloric acid in the fasting juice, but none during the fractional test meal; also in one instance, the amount of free acid in the fasting juice, exceeded the amount present during the test meal. This demonstrates the effect the psychic state of the individual may have on the gastric secretion, for all of these 5 babies attended for the re-examination as out-patients, the fasting juice was secreted before they arrived at the hospital and were in the care of their mother. During the test meal, they were separated from their mother, and found themselves alone in now strange and unfamiliar surroundings.

In 11 of the 14 infants, the amount of free acid found in convalescence, either in the fasting juice or after the gruel stimulus, was greater than during the acute illness. The remaining 3 infants, when in the acute stage of their infection, had all secreted free hydrochloric

acid in amounts above the maximum figure found in normal children of the same age.

Four of these convalescent infants had been examined previously with a combined gruel and histamine stimulus, as they had shown achlorhydria during the acute infection. One (No. 21) secreted no free hydrochloric acid with the combined test meal, but showed a good quantity of free acid in the fasting juice in convalescence. The remaining three (Nos. 1, 14 and 42) showed a greater secretion of free acid during convalescence than had been given with the combined stimulus previously. A gruel test meal given along with histamine dilutes the gastric juice to a varying extent, and may obscure the full response of the mucosa to the maximum stimulus of histamine. However, in these 4 infants the same quantity of gruel was given on both occasions, and thus the same diluting effect should be present. These findings indicate, therefore, that the power of the gastric mucosa to secrete free hydrochloric acid during acute gastro-enteritis is low, even with a maximum stimulus, but that there is a marked recovery during convalescence, so that even with a weaker stimulus, a better response is evoked.

A Percentile Curve of the time of maximum secretion of free acid was drawn from the test meal results of the convalescent and recovered infants who secreted free acid during the fractional test meal of gruel, i.e. 11 results from 10 infants. (Table XV)

Table XV. Time of maximum secretion of free acid during test meal in convalescence.

Time of maximum secretion of free acid during test meal.	Number of infants.	% of total infants having free acid during test meal.
½ hour specimen	3	27.3
1 hour specimen	4	36.3
1½ hours specimen	2	18.2
2 hours specimen	2	18.2

These infants now showed a much earlier secretion of free acid than when acutely ill.

From Graph VI, it was found that the median time was 48 minutes, and the estimated time of maximum secretion was 48±24¾ minutes. Thus 50% of the convalescent and recovered infants had their maximum secretion of free acid between 23¼-72¾ minutes, after the test meal stimulus was given.

RE-EXAMINATIONS DURING SUBSEQUENT PARENTERAL INFECTIONS.

Two infants who had been acutely ill with gastro-enteritis and had made a good recovery, were re-admitted to hospital at a later date suffering from acute parenteral infections. A further investigation of their gastric function was undertaken, using a fractional test meal of gruel. A complete test of all the results from each infant is given in Table XVI.

One infant (No. 1) showed achlorhydria with a gruel test meal during acute gastro-enteritis, though some free acid was noted in response to a combined gruel and histamine stimulus. In convalescence there was recovery of hydrochloric acid secreting power to within normal limits,

Table XVI. Gruel test meal repeated in Parenteral Infection.

Name.	Interval after 1st. test meal.	Method used.	Fract'n'l test meal Free acid mN.	Total acid mN.	Remarks.
1.E.D.	-	Gruel.	0	23.0	Ac. gastro-enteritis.
	2 days.	Gruel & Hist-amine.	6.5	28.0	" "
	27 "	Gruel.	8.0	50.0	Well.O-pat.
	8 wks.	Gruel.	0	22.0	Ac. bronchitis
	17 "	Gruel.	0 (0)	19.0 (91.5)	Well.O-pat. (Fasting juice)
48.H.M.	-	Gruel.	0	17.0	Ac. gastro-enteritis.
	36 days.	Gruel.	0 (7.0)	37.0 (56.0)	Well.O-pat. (Fasting juice)
	16 weeks	Gruel.	20.0	47.0	Ac. otitis med.

though it disappeared again with a subsequent parenteral infection. After recovery from this attack, free hydrochloric acid was again noted in the gastric contents.

The other infant (No. 48) had no free hydrochloric acid in the gastric contents during acute gastro-enteritis, though free acid was found in the fasting juice in convalescence. During an acute parenteral infection in this case, the secretion of hydrochloric acid was not reduced.

COMMENTS.

Acute gastro-enteritis as a clinical entity has been recognised for centuries. The development of bacteriology following the work of Pasteur lead to the separation of certain types of cases as separate diseases, e.g. dysentery, but there still remains a pool of cases in which no specific organisms can be persistently isolated from the stool, and it is these which are included in the term acute primary gastro-enteritis.

Bacteria can readily enter the alimentary tract both from the mouth, which contains a heterogenous flora, and in the feeds, if they become contaminated in any way. The growth of many species of bacteria is possible in the conditions which exist in the alimentary tract, with regard to temperature, moisture, and the nature of the intestinal contents.

In vitro cultures of intestinal bacteria have been extensively studied, but knowledge of these organisms in vivo is limited, especially with regard to the effect of the various enzymes and secretions of the alimentary tract.

Cruickshank et al (20) state that Billroth was the first to observe that the alimentary tract of the newborn baby was sterile. Even up to 30 hours after birth, the bacteria in the meconium are scanty. The intestine soon becomes invaded by a mixed collection of organisms representative of the bacteria in the infant's environment,

which by the end of the first week are in turn replaced by B. bifidus, these constitute 90-95% of the bacteria in the faeces as long as the child is breast fed. Coliform organisms and enterococci (S. faecalis) can be demonstrated on culture. Spore bearing organisms are not commonly present in the intestinal flora of a breast fed baby.

In contrast, the faeces of the artificially fed infant show a very mixed flora, in which are present Gram-negative coliform organisms, Gram-positive bacilli and cocci, and less numerous spore-bearing organisms and Gram-negative cocci. There is no constant proportion.

As the infant grows older and is weaned, the variety of faecal organisms increase. Coliform organisms now form a large proportion of the flora, and the aciduric group are only sparsely represented, spore-bearing organisms are numerous and Gram-positive cocci are always present. There is a wide variation in normal individuals, which makes the classification of abnormal flora difficult.

The acid secretion of the stomach is an important antiseptic in the gastro-intestinal tract. A large number of bacteria must inevitably be swallowed, yet if the hydrochloric acid in the gastric secretion is normal, a degree of acidity is quickly reached, which kills off most organisms except the acid resistant ones, e.g. yeast, tubercle bacillus. Marriott and Davidson (62) noted marked inhibition of the growth of colon, dysentery, and the typhoid

group at pH 5, and complete inhibition and death of the organisms at pH 4. In the beginning of the duodenum, the re-action of the contents is naturally dependent on the secretion of the stomach, thus under conditions of normal gastric secretion bacterial life here is largely inhibited. Davison (23), demonstrated in infants, that the acidity of the duodenum was directly related to the acidity of the stomach. He found one third of the duodenal specimens from normal infants were sterile, the remainder had a mixed flora in comparatively small numbers.

In normal digestion some bacteria will be swept into the intestine, before they have been dealt with by the hydrochloric acid in the stomach. Also, with the swallowing of saliva, independent of meals, organisms may reach the stomach when the acidity is low and enter the intestine unscathed.

As the chyme passes along the bowel, it mixes with the alkaline bile, pancreatic juice and the succus entericus and the increasingly alkaline medium becomes more and more favourable to the growth of bacteria.

In conditions of hypochlorhydria the sterilization of the contents of the upper part of the alimentary tract is not so complete, and in achlorhydria it is almost absent.

The present investigation gave an incidence of achlorhydria in 61% of infants suffering from acute gastro-enteritis, the free acid secretion was below the lower range for normal infants of the same

age in a further 12%. During convalescence and recovery there was a rise or a return of the secretion, and all showed free acid in the gastric contents.

Davison (23) found a heavy growth of B. coli in duodenal cultures of six infants who had died as a result of diarrhoea. In infants convalescent from diarrhoea, the culture showed a small number of organisms mixed in character, B. coli if present were few in number.

Blacklock et al (6) also showed that in infants with acute gastro-enteritis, the normally sterile upper small intestine may harbour a large number of coliform organisms, which have made their way up from the small intestine.

These bacteriological findings are in keeping with the trend of free acid secretion noted in this series, the abnormal ascent of the coliform bacillus being favoured by partial or total inhibition of gastric free acid secretion.

It is believed by some workers that these coliform organisms take on a pathogenic role in their new environment. Goldschmidt (40) demonstrated that they produce a toxic substance on culture outside the body. Dufourt (28) proved experimentally that the coliform bacilli isolated from cases of infantile diarrhoea were more virulent for guinea pigs, than those from normal children. Blacklock et al (6), however, failed to find any particular coliform strain common

to the whole group of their cases of acute gastro-enteritis and absent from cases without enteritis.

Recently Bray (11), Giles and Sangster (39), and Taylor et al (101), working independently, found a close correlation between the same serologically specific type of B.coli and epidemic infantile gastro-enteritis. Rogers et al (89) found that this same organism was often associated with the cases of acute gastro-enteritis which they investigated, but agreed with Taylor et al's conclusions (101) that there was no proof of the actual pathogenicity.

In spite of much work, the aetiology of gastro-enteritis is still a moot point and bacteriological investigations have failed to show any one particular organism to be consistently present. However, there appears to be a definite relationship between the duodenal implantation of coliform organisms and digestive disturbances. In infants the digestive processes are very unstable, and various factors are probably responsible for the disturbance of the intestine, which predisposes to the altered bacteriology.

Irregular peristalsis is common in early life, thus regurgitation of fluid intestinal contents may carry coliform organisms to the upper intestine where they may survive if the acidity is low.

The acidity of the gastric juice, apart from its relationship to the bacteriology of the small intestine is also important in its physiology (94). It was known by physiologists that a flow of

pancreatic juice occurred when the gastric contents entered the duodenum; the same results were obtained when acid was introduced into the duodenum, upper jejunum, or to a less extent in the ileum. More recent work by Mellanby (65) suggests that contrary to previous reports, acid in the duodenum does not give rise to a very profuse flow of pancreatic juice, but that bile is a much more potent stimulus. However, an optimum pH is needed and this is around pH 6.5 or slightly acid. In turn, it has been shown that the pancreatic juice in the intestine is the most effective stimulus to the flow of the succus entericus. Thus the whole process is dependent on an effective acidity of the gastric juice, and deficient secretion of the pancreatic and intestinal juices will occur with diminished or absent free acid secretion in the stomach. This was demonstrated by Davison (23), he found in diarrhoea in infants, that the hydrogen ion concentration of the duodenal contents was increased and the activity of the duodenal amylase and trypsin was diminished. There was an increase in the amylase and trypsin strength of the duodenal contents after marked clinical improvement. This latter fact can be associated with the improved free acid secretion found in convalescence and recovery in the present investigation. Davison states that both Moro (73) and Bessau (5) reported similar results.

The importance of gastric acidity in

initiating peptic digestion must not be forgotten. Pepsin does not begin to act until pH 5.0, it reaches half activity at pH 4.0, and full activity at pH 2.5.

In children with acute gastro-enteritis, the delay in attaining the maximum secretion of free acid in the gastric contents, found in those who secreted free acid during the test meal, must also increase the number of organisms that escape from the stomach into the duodenum, and also delay the enzyme secretion of the pancreas and small intestine. It is important to note that the time of maximum secretion of free acid improved in convalescence and recovery.

As a result of the reduced enzyme activity associated with lowered gastric secretion, there must be an accumulation of undigested and unabsorbed food material in the duodenum and upper jejunum, which provides a rich culture medium. The lower acidity allows invasion of this food material by organisms, either from further down the intestine or from the stomach, where they have escaped the lethal effect of the hydrochloric acid. There will be fermentation of this food material by these organisms with formation of irritating end products, which accelerate peristalsis and cause or increase the diarrhoea.

If this is indeed the sequel of events, then what causes the initial reduction of acidity ? In this series tha majority of the infants were 6 months of age and under - 42 out of 51 -, the larger number being in the second trimester than in the first. Cooper (17) also reported the highest incidence under

6 months of age, with most cases falling in the 3 to 6 months period. Smellie (98) found the highest incidence under 3 months of age. It is generally accepted that the number of cases decline after the age of 6 months and this may be related to several factors.

It has been shown in this investigation that in normal infants the gastric secretion of free acid increases with age. From the age of 6 months, the diet is becoming increasingly varied, and no longer consists exclusively of milk with its strong buffer content. Thus, as the infant grows older, with an increased secretion of hydrochloric acid, there is a reduced intake of a potent buffer containing fluid, so that the free acidity in the stomach will be at a higher level after food, therefore the chain of events just outlined is less likely to occur.

Ylppö (105) suggests that in the production of acute gastro-enteritis, or "Summer diarrhoea", there is an initial rise in temperature due to a mechanical or bacterial cause, associated with sweating. This leads to a lowering of gastric secretion, and sets off the train of symptoms. This may or may not be the explanation. It was observed in the infants examined in this series that the gastric acidity was not influenced by the elevation of the temperature to 100° F. or over, within 24 hours of the test meal being given. However, all the babies had been febrile at some time previously.

Of recent years many unsuccessful attempts have been made to prove that acute gastro-enteritis is a virus infection. Light and Hodes (60) claimed to have isolated from the faeces of affected infants a filterable agent which caused diarrhoea in young calves. It may eventually be proved conclusively that a virus is the precipitating factor.

In this investigation it was found that histamine sometimes failed to produce a secretion of free acid or rise in total acid during the acute infection, whereas the stomach secreted free acid in convalescence with the weaker gruel stimulus alone. All the infants with achlorhydria who were retested in convalescence or recovery, secreted free acid in the fasting juice or during the fractional test meal. Further, there was a return to normal in the median time, and the estimated time of maximum secretion of free acid in convalescence and recovery. It was also noted that in a subsequent parenteral infection, achlorhydria may recur, to be followed again by a free acid secretion in convalescence. These factors will be discussed later in the general discussion.

SUMMARY.

In a study of the gastric functions of infants under 1 year suffering from acute primary gastro-enteritis the following observations were made.

(1) The average free acidity was lowered in all age groups. Individually, the majority of the

infants showed a depression of free acid secretion which was most marked in the older age groups. The combined acidity was high, 61% had achlorhydria, the incidence of this increased with the severity of the illness.

(2) Examination of infants with achlorhydria, using a combined gruel and histamine stimulus, showed that 10.6% still failed to secrete free hydrochloric acid, and there was no rise in the total acidity.

(3) Free acid was present either in the fasting juice or during the fractional test meal in all the infants examined during convalescence or recovery. The amount of free acid increased as convalescence advanced.

(4) During convalescence and recovery infants who had shown achlorhydria with a combined gruel and histamine stimulus, had a good secretion of free acid with the weaker gruel stimulus alone, or if free acid had been secreted during the acute illness there was an improved secretion.

(5) Infants with achlorhydria during acute primary gastro-enteritis, may or may not show achlorhydria in subsequent parenteral infections.

(6) In investigating the time of maximum secretion of free acid the median time was 72 minutes, and the estimated time of maximum secretion

was 45 - 99 minutes, after a test meal stimulus was given. In convalescence and recovery these figures were 48 and $23\frac{1}{4}$ - $72\frac{3}{4}$ respectively.

(7) The emptying time of the stomach tended to be shorter than normal.

ACUTE PARENTERAL INFECTIONS

The children in this group were suffering from parenteral infections, with or without gastro-intestinal upset, and were in the acute stage of the illness when the gastric investigation was carried out. The diseases included otitis media, urinary infections, coryza, pulmonary tuberculosis and whooping cough.

Meyer (68) examined the digestive function of healthy and ill infants using a test meal of gruel and the single aspiration method. He considered that the gastric secretion was unaltered by illness. His results may have been influenced by the fact that some of the infants included in the healthy group were just recovering from alimentary infections, although free of symptoms when the test meal was given.

Chievitz (14) investigated a series of children under one year, by the same method as Meyer (68). Her group of children with alimentary disturbance was very mixed, but cases of coryza, bronchitis, pneumonia and pyuria were included. She observed that half of the infants showed low or absent hydrochloric acid in the test meal, and that sometimes the free acid increased with an improvement in the general condition. In a different group of convalescent children she found a normal secretion of acid. Hertz (44) believed that his work confirmed the results of Meyer, but Chievitz (14) pointed out that Hertz (44) found absent free hydrochloric acid in a good proportion of ill infants and that his findings were more in

agreement with her results.

Müller & Gutschmidt (76) followed up the work of Chievitz (14). They concluded that in parenteral infection with no fever or alimentary upset, gastric acidity was normal, but if either of these symptoms occurred in the course of the disease, the figures for gastric acidity were lowered.

Davidsohn (22) found a rise in pH and a reduced motility of the stomach in influenzal infections, this lasted for some time after the disease.

Marriott & Davidson (62) estimated the pH of the gastric contents after a milk feed in 16 infants, aged 3 weeks to 9 months, and found a deficiency of gastric secretion in these ill children. In a few cases it was possible to demonstrate the fall in gastric acidity from the figure obtained in a previous examination, before the infection occurred. Similar results were obtained by Wills and Paterson (103).

PRESENT INVESTIGATION.

27 infants were included in this group. They were each given a fractional test meal of gruel whilst in the acute stage of their infection.

The results are given in Appendix C and are summarised in Table XVII.

The infants were divided into the same age groups as the normal children, and the average value for free, total and combined acid found for each age period (Table XVIII, Graph VII).

Table XVII Gastric Acidity. Acute Parenteral Infections.

Name	Age in weeks.	Disease	Fasting Juice		Fract'n'l test meal		
			Free Acid mN	Total Acid mN	Free Acid mN	Total Acid mN	Comb'd Acid mN
1.C.C.	5	Ac.Coryza	0	13.5	0	45.0	45.0
2.R.B.	6	Ac.Ot.Med.	0	52.0	33.0	53.0	20.0
3.J.T.	6	Pneumonia	0	56.5	0	74.0	74.0
4.G.H.	7	Pneumonia	1.0	15.0	21.0	30.0	9.0
5.S.H.	8	Pyuria	0	44.0	0	42.0	42.0
6.R.M.	8	Pneumonia	0	8.0	0	17.0	17.0
7.D.C.	9	Pneumonia	3.0	35.0	5.0	25.0	20.0
8.R.L.	9	Pneumonia	0	A	6.5	42.0	35.5
9.S.R.	11	Pneumonia	2.0	118.5	10.0	49.5	39.5
10.R.M.	13	Ac.Ot.Med.	0	A	26.0	43.0	17.0
11.J.M.	15	Pul.T.B.	0	36.0	6.0	32.0	26.0
12.A.G.	15	Whooping C.	0	33.5	5.0	24.0	19.0
13.S.F.	15	Pneumonia	0	A	5.5	31.5	26.0
14.G.M.	18	Ac.Ot.Med.	0	3.5	0	11.5	11.5
15.H.A.	22	Ac.Coryza	0	26.5	0	11.0	11.0
16.F.S.	23	Ac.Ot.Med.	0	10.0	4.0	20.0	16.0
17.R.R.	26	Pneumonia	0	A	10.0	27.0	17.0
18.M.C.	30	Pneumonia	0	9.8	16.0	58.0	42.0
19.P.H.	30	Pneumonia	/	/	0	41.0	41.0
20.J.M.	31	Pneumonia	0	17.0	0	28.0	28.0
21.T.K.	32	Pneumonia	0	3.0	0	11.0	11.0
22.D.K.	34	Pneumonia	0	3.0	6.5	25.0	18.5
23.R.B.	36	Pneumonia	0	13.0	7.0	54.0	47.0
24.C.H.	38	Ac.Ot.Med.	0	A	18.0	49.5	31.5
25.D.C.	38	Pneumonia	0	71.5	8.5	31.0	22.5
26.P.K.	40	Pneumonia	18.0	64.0	7.0	32.0	25.0
27.R.M.	47	Pneumonia	0	A	0	16.0	16.0

A = Amount of gastric contents sufficient only for qualitative test for free hydrochloric acid.
/ = Stomach empty.

Table XVIII. Gastric Acidity. Average in Age Groups.

Age in weeks.	No. of in-fants.	No. with achlor-hydria	Fractional Test Meal		
			Free Acid mN	Total Acid mN	Comb'd. Acid mN
3-4	0	-	-	-	-
5-12	0	4	8.39 ± 3.62	41.94 ±5.30	33.55
13-26	8	2	7.06 ± 2.75	25.00 ±3.59	17.94
27-39	8	3	7.00 ± 2.34	37.19 ±5.36	30.19
40-52	2	1	3.50 ± 2.47	24.00 ±5.66	21.50

In acute parenteral infections, 37% of the infants showed achlorhydria. The average free acid was below normal in all age groups, the difference being greater as age advanced.

At 5-12 weeks the depression below the average normal value was 4.49 mN, at 13-26 weeks it was 7.40 mN, at 27-39 weeks 9.90 mN, and at 40-52 weeks 16.35 mN.

As in acute gastro-enteritis, the climbing curve of free acidity associated with increasing age was absent, though the reduction in free acid secretion was not so great in parenteral as in enteral infections, and the number of infants with achlorhydria was less than half.

Reviewing the case in Table XVII individually, apart from the general trend, it was found that 43% of the infants gave free acid values within or above the normal range for their age.

The total acidity was variable, but the combined acidity tended to be higher than normal.

The range of values for free, total and combined acid was increased.

As in acute primary gastro-enteritis a rise of temperature to 100°F during the 24 hours before the fractional test meal, did not cause any consistent variation in the free or total acidity, compared with infants who were afebrile during this period. All of the infants had been febrile at some time in their illness, before the gastric function was investigated.

Gastro-intestinal symptoms and Gastric Acidity.

It is well known that in infants, gastro-

intestinal upset is frequently present in all forms of parenteral infection and it was thought that variations in the gastric secretion might be associated with this.

16 of the 27 infants had alimentary symptoms accompanying the acute parenteral infection. 7 had both diarrhoea and vomiting, 7 had diarrhoea only, and 2 vomiting only.

Table XIX Gastro-intestinal Symptoms and Gastric Acidity.

Alimentary symptoms	No. of Infants	Fractional test meal	
		Free Acid mN	Total Acid mN
Vomiting	2	11.50	36.75
Vomiting & Diarrhoea	7	11.43	29.93
Diarrhoea only	7	5.50	31.29
None	11	4.86	38.27
Total infants	27	8.84	31.38

It was found that vomiting alone or with diarrhoea was related to high free acidity. With diarrhoea alone or no alimentary upset the free acid was much lower. It would appear, therefore, that vomiting is associated with a raised free acid value in the gastric contents.

Time of Maximum Secretion of free acid.

Table XX Time of maximum secretion of free acid during test meal.

Time of maximum secretion of free acid	No. of Infants.	Percentage of total infants having free acid during test meal.
½ hr. specimen	3	17.6
1 hr. "	6	35.3
1½ hr. "	8	47.1
2 hrs. "	0	0

A Percentile Curve drawn from Table XX, showed that in acute parenteral infections, the median time was 57 minutes, and the interquartile range was 37½ - 75 minutes, (Graph VIII), thus 50% of the group had their maximum secretion of free acid 57 ± 18¾ minutes after the test meal stimulus had been given.

The median time was later than in normal infants though earlier than in acute primary gastro-enteritis. The estimated time of maximum secretion of free acid commenced later and was more prolonged than in normal infants, though again this change was not nearly so marked as in acute primary gastro-enteritis.

The Emptying Time of the Stomach

In acute parenteral infections, in 48.1% of the infants the stomach was empty at 2 hours in contrast with 33.3% in normal children, (Table XXI), thus, the stomach emptied more rapidly in infants suffering from acute parenteral infections than in normal infants. This was also found in acute primary gastro-enteritis, both of which conditions were associated with a lowering of the gastric acidity.

Table XXI Emptying Time of Stomach

Emptying time in hours	No. of Infants	% of Total Infants
Over 2	14	51.9
1½ - 2	8	29.6
1 - 1½	4	14.8
½ - 1	1	3.7
0 - ½	0	0

Fasting Juice

Fasting juice was obtained in 26 out of 27 instances. Free acid was present in 3 cases only, in one of these (No.26) the amount was greater than was found during the test meal; in 5 cases there was only sufficient juice for a qualitative estimation of free acid.

RE-EXAMINATIONS WITH COMBINED GRUEL AND HISTAMINE STIMULUS.

Achlorhydria was present throughout the fractional test meal in 10 out of the 27 infants suffering from acute parenteral infections. A random sample of 5 of these 10 infants were given a fractional test meal of gruel combined with a subcutaneous injection of histamine within 2 days of the first examination. (Table XXII and Appendix C).

Table XXII. Gastric Acidity with combined gruel and histamine stimulus.

Name	Fractional Test Meal		
	Free acid mN.	Total Acid mN.	Comb'd.Acid mN.
3 J.T.	10.0	85.0	75.0
14 G.M.	0	12.0	12.0
19 P.H.	15.0	55.0	40.0
21 T.K.	10.0	36.0	26.0
27 R.M.	9.5	30.0	20.5

It was found on this second examination, that only one of these 5 infants now had an absence of free acid during the test meal; in this infant there was little change in the total acidity with histamine, thus confirming that free hydrochloric acid had not been secreted and immediately neutralized.

These results were applied to the series, and it was calculated that only 7.4% of the infants would show achlorhydria with the stronger stimulus.

RE-EXAMINATIONS DURING THE DISEASE AND IN RECOVERY.

The gastric function was followed through the course of the disease and in recovery in 2 cases. Each infant was given a fractional test meal of gruel on two occasions whilst in hospital, and a third time as an out-patient, when recovery was clinically complete.

Infant No.20, ill with pneumonia, was re-tested 10 days after the first examination. Consolidation of the lungs was still present on physical examination of the chest. The temperature was up to 101° during the 24 hours before first test meal, there was intermittent fever in the interval, but the infant was afebrile for 3 days before the second test meal, and was improving. The third examination was made 6 weeks after the first, the chest was clear and the infant well.

Infant No.22 was also suffering from pneumonia. The first and second test meals were given when the child was ill and febrile and there were marked physical signs in the chest. The third test meal was given 5 weeks after the first, the lungs were not yet

completely clear, but the general condition of the infant was good.

The results of all the gastric investigation on both infants are given in Table XXIII.

Both infants had been acutely ill with pneumonia for 5 days before the first test meal was given and were equally ill.

Table XXIII Gruel Test Meal. Repeated during disease and in recovery.

Name	Interval after 1st. examination	Fractional Test Meal Free Acid mN	Total Acid mN
20 J.M.	-	0	28.0
	10 days	0	25.0
	6 weeks	14.0	43.5
22 D.K.	-	6.5	26.0
	11 days	0	12.0
	5 weeks	9.5	28.5

It was found that there may be individual variations in the development of achlorhydria, for one infant showed no free acid on the first gastric investigation on the fifth day, whilst achlorhydria was not found in the other infant until the second test meal on the sixteenth day of the illness.

Both showed recovery of secretion with the clearing of the lung consolidation and regaining of good health, though the rise of acidity was greater in one than in the other.

COMMENTS.

It was found in acute parenteral infections in infants under one year of age that the average gastric acidity was lower than normal, and that the incidence of achlorhydria was 37%. The hypochlorhydria was not so marked as in acute primary gastro-enteritis and the incidence of achlorhydria lower. Considering

the cases individually it was found that 43% of the infants gave free acid figures within or above the range for normal children of the same age, whereas this figure was only 27% in acute primary gastro-enteritis. It was calculated that 7.4% of the infants with acute parenteral infection would show lack of hydrochloric acid secretion with the combined gruel and histamine stimulus, compared with 10.1% in acute primary gastro-enteritis.

The time of maximum secretion of free acid was earlier in acute parenteral infections, and the estimated time of maximum secretion was shorter and started earlier than in acute primary gastro-enteritis.

16 of 27 infants or 59% had gastro-intestinal symptoms associated with their parenteral infections. Infants suffering from vomiting with or without diarrhoea, showed a larger amount of hydrochloric acid in the gastric contents, compared with those displaying diarrhoea alone or with no gastro-intestinal symptoms. This agrees with Davison's statement (24) that vomiting increases acidity. Wills and Paterson (103) also noted this. Chievitz (14), however, considered that vomiting occurred more frequently in infants with low free acidity; it would appear that she included children with diarrhoea and/or vomiting in one group.

The important point clinically in parenteral infections is that, although the diarrhoea and vomiting should be treated, if present, unless the primary illness is dealt with, treatment of the alimentary

upset is likely to be ineffective. In gastro-enteritis, diarrhoea and vomiting are part of the primary illness.

Ylppo's experimental work (105) on the effect of artificial elevation of temperature in infancy, showed that gastro-intestinal symptoms did not occur in every case with fever. Some infants showed no abnormal effects even with high fever; others showed a decrease in the gastric acidity, but no gastro-intestinal disturbance. A third group showed diminished gastric secretion and diarrhoea. It would appear likely that it is the last group who develop diarrhoea and vomiting in association with parenteral infections, in the present investigation there was very little difference in the gastric acidity in infants with diarrhoea and those with no gastro-intestinal disturbance.

Various reasons have been put forward to explain the relationship of elevation of temperature on gastric acidity. Chang (13) said it was due to cloudy swelling of the cells of the stomach. Ryle (92) believed that the gastric symptoms at the onset of fever point to the action of toxins on the gastric mucosa. Faber (31) in discussing the importance of febrile disease as causing complete suppression of gastric secretion, said that there was a gastritis. It was noted in this investigation that the combined gruel and histamine stimulus failed to produce a secretion of free acid during the acute infection in 7-10% of the cases in acute enteral and parenteral infection. Chang (13) in his series of febrile adults

also used histamine, and had similar results, though he found that 31% had achlorhydria during the acute infection and fever. It would appear that influence of fever on the gastric secretion is most important at the onset of the disease, for it could not be shown in this series that an elevation of the temperature per se influenced the gastric acidity in a consistent way during the actual course of the disease, either in primary gastro-enteritis, or in parenteral infections, but all the infants had been febrile earlier.

Blacklock et al found (6) in infants dying from parenteral infections, that coliform bacilli were increased in the duodenum and jejunum, though less abundant than in acute gastro-enteritis. This can be associated with a less marked depression of gastric secretion, and thus not so great a lowering of the acidity in the intestine.

It must also be borne in mind, that young children swallow the alkaline mucoid secretion from an inflamed naso-pharyngeal mucosa or respiratory tract. Apart from the mucus lowering the gastric acidity by neutralization of the free acid, organisms will also be swallowed, and it is significant that in cases dying of broncho-pneumonia there was a greater incidence of staph.aureus and streptoccoci in the small intestine, than in other groups examined by Blacklock et al (6).

It is reasonable to suppose that in acute parenteral infections, the associated general toxaemia and/or raised temperature produces toxic changes in

the cells of the gastric mucosa. In some individuals this results in a depression, either complete or partial, of the acid secretion. Associated with this depression of free acid secretion, the sequence of events may be started which were outlined in the discussion on acute primary gastro-enteritis, resulting in gastro-intestinal disturbance in susceptible individuals. Vomiting causes frequent emptying of the stomach and in this way may produce irritation of the mucosa and increased acidity, or alternatively, the higher free acid figures may be related to the removal of the food which acts as a buffer.

SUMMARY

In an investigation of the gastric function in acute parenteral infections, the following conclusions were reached:-

1. The average free acidity was lowered in all age groups, the effect was most marked in the older infants. Individually 37% showed achlorhydria, 43% gave free acid values within or above the normal range for their age.
2. The examination of infants with achlorhydria using a combined gruel and histamine stimulus showed that 7.4% ~~would~~ fail to secrete free hydrochloric acid.
3. Vomiting increases the gastric acidity.
4. There is an individual variation in the time of development of achlorhydria in infants equally ill, and also in the degree of the return of the free acid secretion which occurs in recovery from the

disease.

5. In investigating the time of maximum secretion of free acid, the median time was 57 minutes. The estimated time of maximum secretion was $38\frac{1}{4}$ - $75\frac{1}{4}$ minutes after the test meal stimulus had been given.
6. The emptying time of the stomach was shorter than normal.

PYLORIC STENOSIS

Barling & Parsons (3) investigating pyloric stenosis in infants, observed milk clot and mucin in the fasting juice 3 hours after the previous feed, together with a high free and total acidity. With a fractional test meal of gruel or milk, there was usually a high free and total acidity and prolonged emptying time, occasionally up to 5 hours.

Salmi (93) studied 33 infants suffering from the disease, using a test meal of breast milk. He concluded that there was a tendency to hypoacidity, as he found lowered values for both free and total acid in the fasting juice, and after the meal, compared with normal infants.

Miller (72) followed 3 cases of pyloric stenosis, where, prior to the onset of symptoms, gastric secretion was normal in quantity and acidity after a test meal of milk. When the symptoms developed, there was considerable delay in the emptying of the stomach, and he was led to believe that the free and total acid was raised at the onset of the disease, but that achlorhydria developed later; the combined acid was persistently raised.

PRESENT INVESTIGATION.

In this series, 10 true cases of pyloric stenosis were examined. Three infants were treated surgically, and the test meal was given before the operation was performed; six infants were treated conservatively with eumydrin, and they were all given a test meal within 3 days of admission to hospital.

The remaining case, No.6, is of interest, in that the diagnosis was made post-mortem, repeatedly unsuccessful attempts having been made to feel the pyloric tumour, and to demonstrate gastric peristalsis during the four weeks the baby was in hospital before death.

The results are summarised in Table XXIV (and Appendix D.)

Table XXIV. Gastric Acidity. Pyloric Stenosis.

Name	Age in weeks	Fasting juice		Fractional Test Meal		
		Free Acid mN	Total Acid mN	Free Acid mN	Total Acid mN	Comb'd. Acid mN
1.J.B.	3	20.5	98.0	23.5	36.5	13.0
2.R.M.	4	0	72.5	6.0	63.5	57.5
3.D.B.	4	0	10.0	7.0	41.5	34.5
4.R.S.	5	0	32.5	0	75.0	75.0
5.A.M.	6	1.0	97.0	25.0	47.0	22.0
6.T.S.	8	0	103.5	20.5	110.0	89.5
7.W.C.	8	0	12.4	30.0	47.0	17.0
8.T.D.	8	0	110.0	0	60.0	60.0
9.J.M.	8	29.0	77.5	32.0	61.5	29.5
10.J.H.	12	31.5	104.0	38.5	52.5	14.0

Table XXV. Gastro Acidity. Average in age groups.

Age in weeks	No. of infants	Fractional Test Meal		
		Free Acid mN	Total Acid mN	Comb'd. Acid mN
3-4	3	12.17±4.64	47.17±6.87	35.00
5-12	7	20.86±5.43	64.71±7.77	43.85

No child in this group was over 12 weeks or under 3 weeks of age. Comparing the results with the 3-4 weeks and 5-12 weeks age-group of the normal series, it was found that the average free, total and combined acidities during the fractional test meal were all markedly raised in pyloric stenosis (Table XXV), and also that the range of free and total

acidity was much wider. Seven of the ten infants gave figures for free acid greater than the maximum for the same age group in normal infants.

All ten babies had a raised total acidity compared with the normal children and the combined acidity reached very high values in some instances.

The values for free and total acidity tended to increase as the disease persisted. (Graph IX). This rise may be influenced by age to some extent, for higher free and total acid values were encountered in the older group of babies, however, it is a possibility that the older child may have had the disease longer than the younger one, before coming for treatment.

Baby No.6 was examined twice, first at the sixth week of the disease when aged 8 weeks, and again one-and-a-half weeks later, a fractional test meal of gruel was given on both occasions. (Table XXVI).

Table XXVI. Gruel Test Meal repeated during disease in baby No.6.

Intervals after onset of symptoms.	Fasting juice		Fractional Test Meal		
	Free Acid mN	Total Acid mN.	Free Acid mN	Total Acid mN	Combined Acid mN.
6 weeks	0	103.5	20.5	110.0	89.5
7½ "	10.0	57.0	60.0	76.0	16.0

Although this case was not diagnosed antemortem, the test meal findings of high, free, total and combined acidity in both instances, were characteristic of the results in the other cases of pyloric stenosis.

Achlorhydria was found in 2 of the 10 cases examined, one baby (No.4) had been ill for two weeks, and the other (No.8) for four weeks.

Baby No.8 was retested on the day after the first test meal, using a fractional test meal of gruel, combined with a subcutaneous injection of histamine. Achlorhydria was present at this examination also; there was little change in the total acidity, indicating that no free acid had been secreted and neutralised. (Table XXVII). Unfortunately distance did not permit the bringing of this infant for another examination at a later date after discharge from hospital.

Table XXVII. Repeat fractional test meals in babies No.4 and No.8.

Name	Interval after 1st. test meal.	Method Used	Fasting Juice		Fractional Test Meal		
			Free Acid mN.	Total Acid mN.	Free Acid mN.	Total Acid mN.	Comb'd Acid mN.
No.4	7 weeks	Gruel	0	38.5	6.0	48.0	42.0
No.8	1 day	Gruel + Histamine	0	93.0	0	65.0	65.0

Baby No.4, though not tested with the combined gruel and histamine stimulus, was re-examined with a fractional test meal of gruel seven weeks later, when twelve weeks old. She was gaining weight steadily, vomiting had ceased six weeks previously. At the second examination, free hydrochloric acid was found to be present, the figure was within the normal range, but below the average for a child of twelve weeks.

Time of maximum secretion of free acid.

8 infants secreted free hydrochloric acid during the fractional test meal.

Table XXVIII. Time of maximum secretion of free acid during test meal.

Time of maximum secretion of free acid.	Number of Infants	% of total infants having free acid during test meal.
½ hour specimen	1	12.5
1 hour specimen	1	12.5
1½ Hrs. specimen	2	25
2 hours specimen	4	50

The Percentile Curve (Graph X) drawn from Table XXVIII gave the median time as 90 minutes and the interquartile range as 60-108 minutes. It was calculated from this curve that 50% of the children had their maximum secretion of free acid 90± 24 minutes after the test meal stimulus had been given.

Compared with normal children, the median time and the estimated time of maximum secretion was doubled.

The Empything Time of the Stomach

The test meal was discontinued after two hours and no investigations were made later than this; in only one instance did the stomach empty in under two hours.

The resting juice aspirated after a seven hour fast was greatly increased in amount, and sometimes showed milk clots, thus also indicating a prolonged emptying time.

Fasting Juice

Fasting juice was present in all cases, it was greatly increased in amount, and measured 20 c.c. or over in 60% of the infants. Free acid was absent in six infants, or three-fifths of the cases, in one of these free acid was not secreted during the

fractional test meal. The total acid was high, and in six of the ten infants higher figures were recorded in the fasting juice than during the test meal. The combined acid figures were all raised.

COMMENTS.

In pyloric stenosis there is gastric stasis and persistent vomiting due to obstruction to the passage of food from the stomach caused by hypertrophy of the circular muscle fibres at the pylorus.

Foster and Lambert (35) studied dogs with artificially produced pyloric stenosis. They found prolonged secretion by the gastric glands with lengthening of the digestive period, and a decrease in the amount of the hourly secretion.

Wills and Paterson (103) noted an increased gastric acidity in infants (aged 2-9 months) with persistent vomiting. Davison (24) in examining a group of older children, found that the gastric acidity was raised in those with vomiting. He suggested that this was due, either to the fact that in the non-vomiting group the gastric contents were unbuffered by the food residue, or that the frequent emptying of the stomach stimulated the gastric mucosa to excess secretion of acid.

In the physiology of gastric secretion, there are known to be three phases, a psychic phase, and two chemical phases - gastric and intestinal. The psychic phase is initiated by the thought, smell, taste, etc. of food, before the food reaches the stomach. The intestinal phase commences when the food has passed

into the small intestine. The gastric phase begins when the food enters the stomach and the secretion is activated by the direct stimulus exerted by the food on the gastric mucosa; it is believed that a secretagogue hormone is released, which is transmitted by the blood steam to act on the cells which elaborate the gastric juice (61). Pavlov (82) denied that mechanical factors play a role in the gastric phase, but Ivy and McCarthy (52) observed an increase in secretion after distending the stomach with air.

In pyloric stenosis, the delayed emptying time means that the food remains in the stomach longer than normal, thus it is possible for there to be a prolonged release of the secretagogue hormone, resulting in a prolonged secretion and a high acidity. The fact that the maximum secretion of free acid is more intense and later than normal, is strongly suggestive that the secretion is prolonged.

Bile is never present in the stomach in pyloric stenosis, this is an important point clinically in the differential diagnosis. Its absence indicates that no duodenal regurgitation occurs through the obstructed pylorus, this was also proved by Parsons (81) in estimations of the total and mineral chlorides. The effect of duodenal regurgitation on gastric acidity has given rise to much discussion. Boldyreff first introduced the theory that duodenal regurgitation was an important factor in the reduction of gastric acidity; he considered

that it was an automatic process, based on the inability of the duodenum to tolerate a fluid more acid than 40 mN. Shay, Katz and Schloss (95) after a careful study of the problem, concluded that duodenal regurgitation does take place, but that the duodenal fluid is not sufficiently alkaline, and regurgitation is not regular enough, to affect the gastric acidity to any great extent. They showed, as did McLean and Griffiths (64), that the acidity falls, even if no duodenal regurgitation takes place. Davison (24) considered that duodenal regurgitation was an important factor in children.

In pyloric stenosis, absence of duodenal regurgitation may be a contributory factor to the high acidity. A more important factor appears to be the prolonged presence of food in the stomach, causing a continued secretion of acid, and this accumulates in the absence of emptying; vomiting may be an accessory factor.

It was found that the longer the duration of the symptoms, the higher the figures for free and total acid. This was not true in all cases, as two babies showed achlorhydria. One of these infants was able to secrete free hydrochloric acid during the test meal given seven weeks later, when recovery had been complete for some weeks. Thus it appears that, though hyposecretion and achlorhydria may occur, as found by Miller (72), the gastric mucosa can recover its acid-secreting power.

Summary.

The following observations were made on the

gastric function in pyloric stenosis in infancy:-

(1) The average free, total and combined acidity was high.

(2) The acidity tends to rise with duration of the symptoms, though achlorhydria may occur.

(3) Two of the ten infants had achlorhydria during the fractional test meal. The free acid secretion was shown to return after recovery.

(4) The estimated time of maximum secretion of free acid following a fractional test meal of gruel was 90 ± 24 minutes.

(5) The fasting juice was increased in amount, and showed a high free and total acidity.

INFANTILE ATROPHY.

This nomenclature covered a group of infants who were all under-nourished to a greater or lesser degree. They may or may not have had loose stools and/or vomiting at home. On admission to hospital these infants were vigorous, non-toxic, non-dehydrated, and apart from signs of wasting and neglect, clinical examination was negative.

Parsons (81) in his investigation of gastric acidity in infantile atrophy found free hydrochloric acid present in the great majority of cases, but the values were variable, and in a few cases, no free acid was demonstrated. Marriott and Davidson (62) in their study of a group of children under 1 year, considered that in nutritional disturbances, the acidity of the gastric contents was lower than in normal infants. Wills and Paterson (103) agreed that in underweight infants, gastric acidity was reduced. In both sets of investigations, milk feeds were used to stimulate gastric secretion. Chievitz (14) included cases of infantile atrophy in her series of infants with alimentary disturbances. More than half of the group showed low or absent hydrochloric acid after a test meal of gruel. Müller & Gutschimdt (76) studied 18 cases of infantile atrophy by the single aspiration method, after a test meal of gruel. Thirteen babies had achlorhydria, in four the acid secretion was low, and in one it was raised above normal. In some cases with achlorhydria, a low secretion of free acid was noted with improvement in the general condition.

PRESENT INVESTIGATION.

In this series the gastric function of 10 infants was examined using a fractional test meal of gruel (Table XXIX). A summary of each case history is given in Appendix E., along with the full results.

Table XXIX. Gastric Acidity. Infantile Atrophy.

Name.	Age in wks.	% under expected weight.	Fasting Juice. Free Acid mN.	Fasting Juice. Total Acid mN.	Fract'n'l Test Meal Free Acid mN.	Fract'n'l Test Meal Total Acid mN.	Fract'n'l Test Meal Combined Acid mN.
1.J.L.	5	34	4.0	12.5	12.0	29.0	17.0
2.E.P.	5	38	0	72.0	20.0	69.0	49.0
3.E.C.	7	30	00	A	16.0	28.0	12.0
4.R.S.	8	42	0	45.0	0	42.0	42.0
5.E.W.	8	22	17.0	57.0	26.0	76.0	50.0
6.S.M.	9	41	32.5	66.5	19.0	36.0	17.0
7.C.M.	10	29	0	16.0	11.3	62.0	50.7
8.J.D.	14	38	0	24.0	45.0	57.5	12.5
9.J.R.	15	27	0	A	19.5	41.5	22.0
10.J.H.	16	33	0	60.0	14.0	30.0	16.0

A = amount of gastric contents sufficient only for qualitative test for free hydrochloric acid.

It was found that the average free acid in babies 5-16 weeks old, diagnosed as Infantile Atrophy, was 18.28 ± 3.50 mN, the average total acid was 47.10± 5.30 mN, and the average combined acid was 28.82 mN. These figures in normal infants aged 5-16 weeks were 13.05±2.17 mN, 33.72±2.37 mN, and 20.67 mN. respectively. Thus, in infants suffering from Infantile Atrophy, the free, total and combined acidity was raised, and the range was wider.

In seven of the ten infants the free acid values were higher than the average figure in normal children, and in two, the free acid was within normal limits. In the remaining infant achlorhydria was present throughout the test meal, and no free acid was found in the fasting juice, although the combined acidity was high in both instances.

Time of maximum secretion of free acid.

Two-thirds of the infants who showed free acid during the fractional test meal, had their maximum secretion within 1 hour of the test meal stimulus.

Table XXX. Time of maximum secretion of free acid during test meal.

Time of maximum secretion of free acid.	Number of infants.	% total infants having free acid during test meal.
½ hour specimen	2	22.2
1 hour specimen	4	44.5
1½ hours specimen	2	22.2
2 hours specimen	1	11.1

The Percentile Curve constructed from Table XXX gave a median time of 51 minutes, and an interquartile range of 33 to 70½ minutes (Graph XI); from these figures it can be calculated that the estimated time of maximum secretion is 51±18¾ minutes, thus 50% of the infants had their maximum secretion of free acid between 32¼ and 69¾ minutes after the test meal stimulus was given.

Compared with normal children, the median time was 7½ minutes later. The estimated time of maximum secretion started only 2 minutes later, but was 10 minutes longer.

Emptying Time of the Stomach.

Table XXXI. Emptying Time of Stomach.

Emptying time in hours.	No. of infants.	% total infants.
Over 2	6	60
1½ - 2	3	30
1 - 1½	0	0
½ - 1	0	0
0 - ½	1	10

The emptying time of the stomach in Infantile Atrophy was similar to normal children, though in one infant, the starch/iodine test was negative half an hour after the start of the test meal.

Fasting Juice.

The amount of fasting juice was normal.

Three infants had hydrochloric acid in the fasting juice, and in one of these, the amount was greater than during the test meal. In five cases the total acidity of the fasting juice was higher than during the fractional test meal.

COMMENTS.

In its early stages loss of weight is due to wastage of fats, or other metabolically inactive tissues; later, there is wasting of muscular or metabolically active tissue. Fleming (33) stated that this later stage was reached when the weight of the child had fallen to 65% of the expected weight for its age. Talbot (100) believed that body metabolism became abnormal at 20% or more below the average weight for the age, and considered that if an infant was 80% or under its expected weight, the condition of infantile atrophy was present. In this present series, Parson's example (81) was followed and all the infants were between 58% and 78% of the average weight for their age.

Fleming's evidence (34) suggests that failure to thrive in atrophic children is not due to

the inability of the organism to utilise any of the proximate principles of food, but rather to an insufficient diet, or to gastro-intestinal disturbances, leading to defective absorption of carbohydrate.

Parsons prefers to believe that absorption of carbohydrate is not abnormal but that there is an excess oxidation of sugar in the body, and a depletion of glycogen reserves. He believes that infantile atrophy (in uncomplicated cases) is primarily due to a supply of unsufficient or unsuitable food, and that once the initial loss of weight to 80% of the expected weight occurs, the continuance of the atrophic state depends on an altered metabolism, and not on disorders of digestion or absorption.

Clinically, it has been found that the giving of acidified milk to atrophic children, brings about an improvement (81), (30), (62).
It has been suggested that acidification reduces the amount of buffer substances in the milk, thus enabling a higher acidity to be reached in the stomach, which allows the gastric enzymes to be more fully activated. Pepsin does not begin to act until pH, 5.0, it reaches half activity at pH 4.0 and full activity at pH 2.5. It has been noted, however, that in infantile atrophy, the absorption of protein is satisfactory (81) (34), which, in turn, must mean that the secretion of hydrochloric acid is sufficient for the initiation of protein digestion by pepsin. This is corroborated by the findings in this series, namely that the gastric acidity - free, total and

combined - was high.

Parsons (81) considered that there was a variation in the acidity, but did not state the tendency of his findings. Marriott and Davidson's (62) and Wills and Paterson's (103) observations of hyposecretion may be associated with the fact that cows milk meals were given.

All the infants, but one, gave a history of gastro-intestinal upset at some time, viz. anorexia, vomiting, loose stools, or constipation. Vomiting was the most frequent symptom, and was noted in eight of the ten infants, loose stools were present in five cases. Such symptoms must interfere with the intake and absorption of food-stuffs, whether or not they are the direct cause of the under-nutrition.

The tendency to high gastric acidity in infantile atrophy is possibly the result of more than one factor. It may be assocated with vomiting (24) (103).

Babbot et al (1) believed that the kind of food determined the amount of acid necessary for digestion, and if the total buffer substance in the food was increased, the acid requirement was increased also. Davidsohn (22) showed that the pH of the stomach contents of artificially-fed infants, varied with the type of food. Parsons (81) demonstrated that different artificial foods have varying buffer values. Thus, if a baby is incorrectly fed, or has its feeds changed from one type of food to another two, three or more times, the gastric acidity may

show some departure from normal in certain infants.

Finally, it must not be forgotten, that there may be an inborn tendency to hypersecretion.

Summary.

The gastric function of infants diagnosed as Infantile Atrophy was examined by a fractional test meal of gruel. The following conclusions were reached:-

1) The average free, total and combined acidity was high compared with normal infants of the same age (5-16 weeks). 70% of the infants had free acid values above the average normal figure.
2) Achlorhydria was found in 1 out of 10 cases.
3) The Percentile Curve for the time of maximum secretion of free acid, gave the median time as 51 minutes, and the estimated time of maximum secretion as $51 \pm 18\frac{3}{4}$ minutes.
4) The emptying time of the stomach showed no departure from normal.

GENERAL DISCUSSION.

In this investigation, a study has been made of variations in gastric function occurring in four common pathological conditions of infancy.

Gruel was chosen as the material for the test meal for several reasons. It can be given to any child without causing alimentary upset, and it is easily aspirated through a narrow bore tube. The motor function of the stomach can be studied by the presence or absence of starch in the fractional specimens. Gruel stimulates gastric secretion satisfactorily, and does not bind much free hydrochloric acid; this low buffering power is important, and is associated with a negligible incidence of achlorhydria in healthy children.

In children, as in adults, histamine is used to differentiate between true and false achlorhydria. Comfort and Osterberg (16) showed that histamine does not always evoke a full response from the acid-secreting cells of the gastric mucosa, and the consistency of the response can be questioned; they noted one case in their series in which an Ewald test meal evoked a free acid secretion, whereas histamine did not; in two other cases, the response from histamine stimulation was smaller than from an Ewald test meal; Gaither (36) agreed with this. On the other hand, Bockhus, Bank and Willard (9) considered that if large enough doses of histamine were given, (sufficient to produce cutaneous erythema), one never failed to

get hydrochloric acid formation, if the mucosa was capable of producing it.

In view of the work of Comfort and Osterberg (16) and of Gaither (36), it was decided to combine gruel with histamine as a test meal stimulus, if it was desired to repeat the gastric investigation of infants showing achlorhydria. The dose of histamine chosen (0.02 mgm. per kilo) was found by Cutter (21) invariably to produce cutaneous erythema in infants. It was realised that there would be some dilution of the gastric contents by the gruel, and perhaps some neutralization of the hydrochloric acid secreted. Any neutralization, however, would be reflected in an increase of the combined and total acidity compared with the first examination, and could be judged accordingly.

The results of the present work, showed that in normal infants, gastric acidity increased during the first year of life. Secretion was low at 3 to 4 weeks, there was a rapid rise in the 1 to 3 month age period, and a much slower rise thereafter. The combined acidity was high in the 1 to 3 month age period, but there was a tendency for it to decrease in the second 6 months of life. Cutter's investigation (21) with histamine showed a similar trend, though the free and total acidity reached much higher figures by 1 year of age.

In acute primary gastro-enteritis and in

acute parenteral infections, the average free acidity was reduced compared with normal, especially in the older age group, the changes were most marked in acute primary gastro-enteritis. Student's "t" test was applied to the results, and the probability of the observed difference between the normal free acid figures, and those found in these two pathological conditions being due to chance were obtained from tables of "t". It was found that from 13 weeks onwards, the difference was increasingly significant, both in acute enteral and parenteral infections, the probability that the difference in the figures for each age group would occur by chance became progressively greater; this was especially so in acute primary gastro-enteritis. (Appendix F).

The total acidity in acute primary gastro-enteritis showed little change from normal, and in acute parenteral infections it was variable; these results were also reflected in the significance tests.

The combined acidity was raised in both of these two disease states.

In pyloric stenosis and infantile atrophy the gastric acidity was raised, the free acid moderately, and the total acidity markedly, especially in pyloric stenosis. Students "t" test showed that the observed difference of the acidity figures from the values obtained in normal infants were highly significant in the case of the total acidity,

especially in pyloric stenosis.

Sixty-six per cent. of normal children required more than 2 hours for the stomach to empty, and the longest emptying time was associated with the highest average figures for free and total acid. Infants suffering from infantile atrophy showed little variation from normal. In pyloric stenosis, the emptying time was prolonged, as would be expected from the obstruction at the pylorus. In acute primary gastro-enteritis 8%, and in acute parenteral infections 15%, fewer children required an emptying time of the stomach of over 2 hours; these conditions were both associated with low average gastric acidity.

Bockhus, Bank and Willard (9) reported in their investigation of normal adults, that the emptying time of the stomach was constant for the same individual with repeat test meals. A study of the present results were made, comparing the emptying time at the first examination with the time found on subsequent test meals. It was concluded that in a large number of infants, the emptying time of the stomach was not constant, either on repeat test meals with gruel, or gruel and histamine given during the acute disease, or on examinations as out-patients in convalescence and recovery.

When gruel is given as a stimulus to gastric secretion, or, indeed, any method used other than a parenteral injection, there is necessarily a dilution of gastric secretion to a varying degree (8).
In recent years, dilution indicators have been introd-

uced to enable corrections for this dilution to be made in the results (50). In the absence of this, the figure given for the maximum free acid secretion during a gruel test meal is not a true one, as it is when histamine is used alone. Further,if specimens are taken off only at half hourly intervals, then the time at which the maximum hydrochloric acid secretion is reached in the gastric contents, may actually be before or after this half hourly interval. However, if the same method is used throughout an investigation the results are comparable, so that one set of results may be compared with the other. We can thus contrast the figures from the Percentile Curves referring to the time of maximum secretion of free acid during the test meal.

It was found that the median time, (or time by which 50% of the infants had their maximum secretion of hydrochloric acid), and the estimated times between which 50% of the infants had their maximum secretion of hydrochloric acid, approached nearest to normal in infantile atrophy. The median time was latest in pyloric stenosis (90 minutes), this was associated with an estimated time of 66 to 114 minutes in which 50% of the children had their maximum secretion of hydrochloric acid; all these times are almost exactly double those in normal infants. The significance of these figures with relation to the high acidity and delayed emptying time, has already been discussed.

In acute primary gastro-enteritis and acute parenteral infections, a later median time and a wider spread of the stimated time of maximum secretion, which also started later, was associated with a low gastric acidity and a high percentage of infants with achlorhydria. This suggests that the response of the gastric mucosa in these disease states is more sluggish, the effect being most marked in gastro-enteritis. It is interesting to note that the figures approached normal in convalescence and recovery from gastro-enteritis, when also the achlorhydria disappeared and the gastric acidity increased. If a larger set of figures had been available, the infants followed-up after gastro-enteritis would have been sub-divided into groups which were related to increasing intervals from the acute infection.

Throughout the whole investigation, it was apparent that a study of the fasting juice was not a reliable method of assessing gastric acidity in infants over two weeks of age, for, in the majority of cases, free acid was absent from the fasting juice, though found during the fractional test meal. It is important that examination of the free and total acidity of the fasting juice should not be omitted, for it was found in the follow-up of some of the "cured" cases, that an appreciable amount of hydrochloric acid might be present in the fasting juice, when there was a psychic depression of free acid secretion during the fractional test meal. Pyloric stenosis was the only condition to

show any gross changes in the fasting juice, when the quantity and total acidity were greatly increased.

The question of congenital achlorhydria has given rise to much argument. There is evidence to show that almost all unfed new born infants have varying amounts of free acid in their gastric secretion (42) (45) (83). This view was not held by Ritter (87) or Miller (71); the latter failed to find hydrochloric acid in the gastric residue of 6 out of 50 normal infants whose fasting juice was examined daily during the first ten days of life, one of these exhibited achylia gastrica two years later after histamine. Miller (71) showed, via the fasting juice, that there is a steady decline in the total acidity of the gastric contents from birth to the tenth day of life. Cutter (21) in his investigation with histamine also found this, and stated that there was probably a fall in acidity after the tenth day of life, with a subsequent increase; he found histamine-fast achlorhydria in 6 out of 15 infants, aged up to 28 days and no secretion whatever followed the giving of histamine in 2 others; in the remaining 55 cases, aged up to 4 years, free acid was always found in the gastric contents after histamine.

Examples of histamine-fast achlorhydria in childhood are rare. Dietrich and Shelby (26) examined 14 children aged 4 to 14 years, and found free acid in every case. Siemsen (97) made 40 tests on children $4\frac{1}{2}$ to 13 years old, and noted achlorhydria in 1 only. Neale (78) studied 29 children from 6 months to 2 years of age, without

finding an-acidity.

Using gruel, Ogilvie (79) demonstrated no case of true anacidity in 60 healthy children aged 6 months to 12 years, neither did Muhl (75) in 40 normal children aged 1-13 years. Chievitz (14) examined over 50 infants, well and ill, and all showed free acid at some time during the first or repeat test meal, no infant was under 2 months of age. Müller and Gutschmidt (76) also using gruel, followed the gastric secretion of 3 young infants, giving repeated test meals; they observed that free hydrochloric acid did not appear until 3 months.

The incidence of achlorhydria in normal infants in this present series was 2 out of 4 infants in the 3 to 4 week old group, all the remaining 20 infants aged 5-52 weeks secreted hydrochloric acid. In Cutter's histamine series (21), all the infants with achlorhydria were also under 5 weeks of age.

The evidence, therefore, shows that at birth congenital achlorhydria is rare. True achlorhydria may occur from 10 days to the end of the fourth week of life, thereafter it is extremely uncommon in healthy children.

Miller (71) compared the fasting juice of mature and premature infants within 8 hours of birth, and noted achlorhydria more frequently with lower birth weight. He made histological studies of gastric mucosa post-mortem and showed that the heavier the infant at birth, the more likely it is to have a more perfectly devloped gastric mucous membrane,

and potent gastric secretion.

The normal increase of gastric acidity during the first year of life, and the individual variations from one infant to another, may be the result of one or more factors. It may be that in some cases the hypoplasia noted by Miller (71) in infants of low birth weight, tends to persist in mature infants. The relative proportion of functionally mature acid secreting cells of the stomach, may be lower than in the adult stomach. The cells may be normal in number, but their rate of secretion may be low because of lack of stimulation or because of specific inhibition. An "adult" number of mature cells may be secreting at their full rate, but the neutralizing mechanism may be operating to excess.

Pavlov (82) introduced the hypothesis that gastric juice as it flows from the gastric glands possesses a constant acidity. Alternatively, Rosemann (90) believed that the chlorine ions brought to the gastric glands are secreted at a definite fixed concentration, partly unchanged as sodium chloride, and partly converted to hydrochloric acid. The extent of the change governs the acidity of the secreted juice.

The work of Hollander and Cowgill (49) supports Pavlov's theory in adults, and this is more generally accepted. Very little work has been done in children.

From Miller's evidence (71), it would appear

that the likeliest factor in the low gastric acidity in infants is that the functionally mature acid secreting cells are relatively less in number in infancy, but that the proportion of these cells increases with age.

The existing evidence indicates that the parietal cells of the gastric glands are responsible for the acid secretion in the stomach; the method of formation of hydrochloric acid by the glands is not yet clear.

Dawson and Ivy (25) from their histological studies put forward two hypotheses, they suggested that the cells form dilute hydrochloric acid within themselves, this diffuses rapidly from the cell to the lumen of the canaliculus, undergoing considerable concentration on its passage through the lumen of the gland. Alternatively, their evidence might be interpreted that the weak acid reaction observed in the parietal cells is due to partial dissociation of the hydrogen and chlorine ions from their precursors, and that complete association only occurs in the canaliculus, or at the surface film separating the cytoplasm of the cells from the lumen of the canaliculus.

The studies of Fitzgerald (32) all tended to show that hydrochloric acid is formed, at least in part, within the parietal cell. She believed it was formed within the cells and that it diffuses into the canaliculus. Hoerr and Bensley (46) believed that whilst the parietal cells may form

precursor of the acid they do not produce the acid itself, merely the neutral chloride, and that the hydrochloric acid is liberated by a hydrolytic process in the neck and foveola of the gland, or within the gastric cavity.

The negative chloride ions come from the neutral chloride of the blood and lymph, for during secretory activity, the blood in the afferent blood vessels of the stomach shows a higher chloride content than in the efferent vessels (10).

The source of the hydrogen ions for acid formation is not clear. Hollander (47) suggests that it can be inferred that hydrochloric acid is derived from an inorganic chloride by interaction with water, carbonic acid, or an acid salt, for concurrent with gastric secretion the blood stream shows an increase in the concentration of total base and CO_2 combining power.

Ryle (92) noted that on a salt free diet, the response to a test meal was not influenced. Evidence in dogs, shows that the parietal cells will continue to function even when the body is no longer able to maintain many of its other activities, so long as the blood continues to supply the gastric glands with water and chloride and removes the waste product from the cell interior (27).

This being so, the question arises as to what changes in the physiology of the stomach are responsible for the high incidence of achlorhydria and hypochlorhydria found in acute primary gastro-

enteritis and acute parenteral infections, and do these changes contribute to the incidence of chronic achlorhydria in adult life, which is estimated to be 4-5% at 20 years of age (7) (80).

During this investigation, in gastro-enteritis 61% of the infants failed to secrete free acid during a gruel test meal in the acute stage of the disease, it was calculated that in 10% of the total infants the achlorhydria was histamine-fast. Furthermore, the more severe the infection and toxaemia, the higher the incidence of achlorhydria. During convalescence and recovery all the infants tested showed a secretion of free acid, even though the achlorhydria had been histamine-fast during the acute infection.

In parenteral infections, 37% of the infants showed absence of free acid during the gruel test meal in the acute stage of the infection, and it was deduced that in 7.4% of the total infants the achlorhydria was histamine-fast. There was a variation in the length of time taken for achlorhydria to develop in children equally ill with the same disease. The ability to secrete free acid returned after recovery from the infection.

When the ability to secrete hydrochloric acid returned after recovery from gastro-enteritis, one infant showed that it could be lost again during a subsequent acute parenteral infection, again with return of the free acid secretion in convalescence.

That a certain percentage of infants with

acute enteral and parenteral infections, failed to secrete hydrochloric acid in response to histamine, indicates that all the parietal cells must be out of action in these particular individuals. The remaining infants, who secreted hydrochloric acid during the gruel test meal, required a longer interval than normal after the stimulus was given to attain the maximum amount of free acid in the gastric contents, suggesting that, in these cases, the parietal cell was not functioning normally. The effect on the parietal cell, however, was not permanent, for all the infants tested in convalescence and recovery were able to secrete hydrochloric acid, and the response to the gruel stimulus was more rapid.

Evidence thus points to a toxic effect on the parietal cell, this is supported by the fact that in acute primary gastro-enteritis the more severe the disease and the toxaemia, the greater the incidence of achlorhydria.

Is the toxaemia of the disease alone responsible for the depression of cellular activity, or are there some additional factors ? In acute parenteral infections toxaemia from the primary disease, together with elevation of the temperature, would explain the occurrence of hyposecretion. In acute primary gastro-enteritis, as discussed previously, the "trigger" factor (associated with reduced gastric acidity) which starts off the pathological train of events in the small intestine

may be fever, or possibly a virus infection, as yet undiscovered.

From histological investigations, Faber (31) reported that direct irritation of the gastric mucosa by the stomach contents, or indirect irritation by toxic agents in the blood stream, produced the same effect on the gland parenchyma of the stomach. Initially there was round cell infiltration of the sub-mucosa, and cloudy swelling of the epithelial cells. If the irritation persisted, lesions of the glands eventually resulted in a decrease in the number, and gradual atrophy.

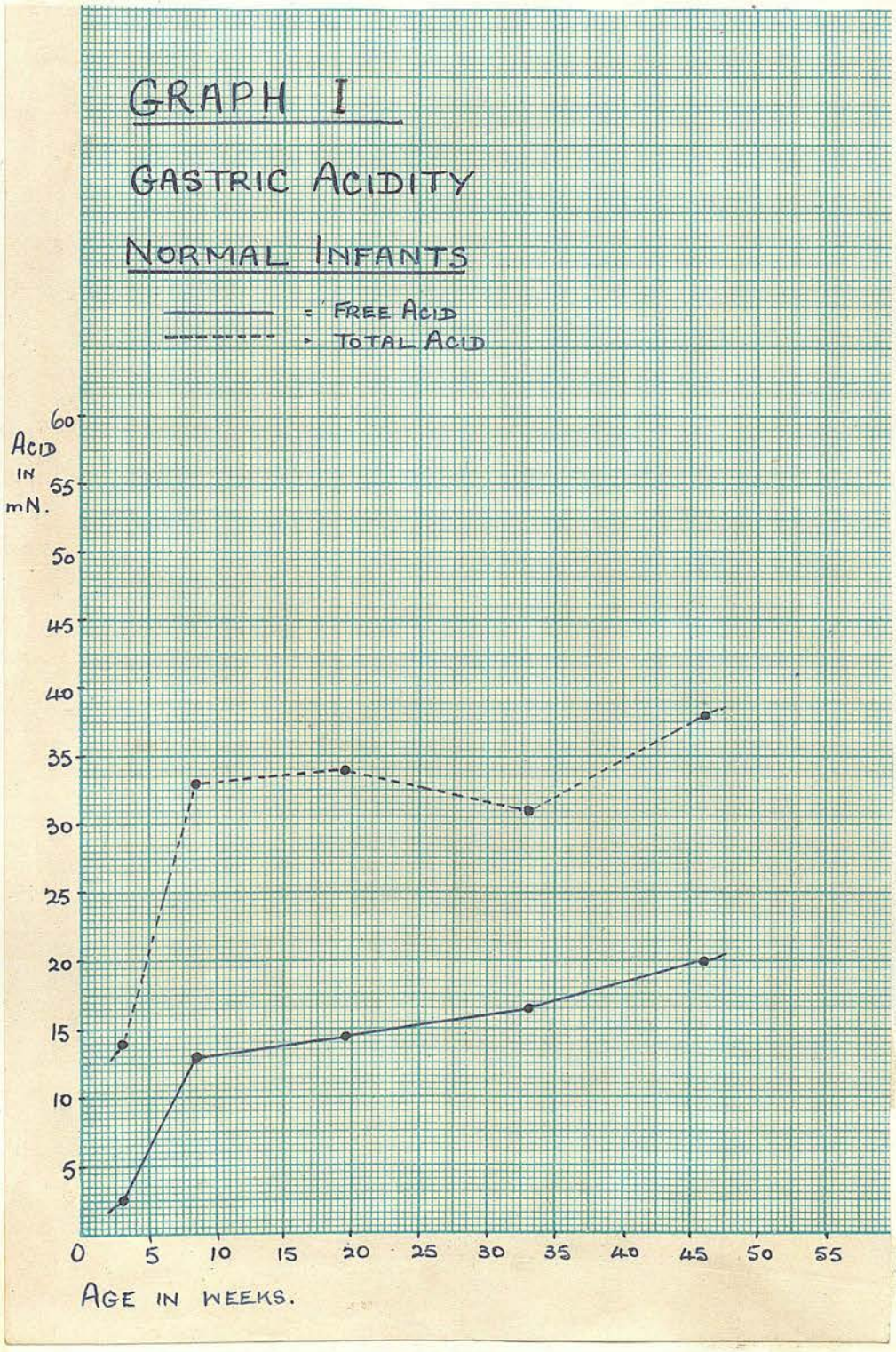
It was found in this series that after recovery of free acid secretion in acute primary gastro-enteritis, a subsequent parenteral infection might again cause achlorhydria, which also cleared up after the parenteral infection subsided; thus the gastric mucosa may be subjected to recurrent trauma.

Dawson and Ivy (25) demonstrated regional activity of the stomach in adults, but it is not known whether this functional reserve exists in the stomach of the very young, though other organs, such as the liver and kidneys, have a functional capacity far beyond the normal requirements of the body.

With recurrent infections occurring from birth, it is reasonable to suppose that in some individuals the parietal cells may not recover completely between attacks, and gradually in increasing numbers become permanently damaged. Considerable natural variation in gastric acidity

is present in normal health, therefore it would be expected that achlorhydria would occur earlier in those who naturally have a low acidity.

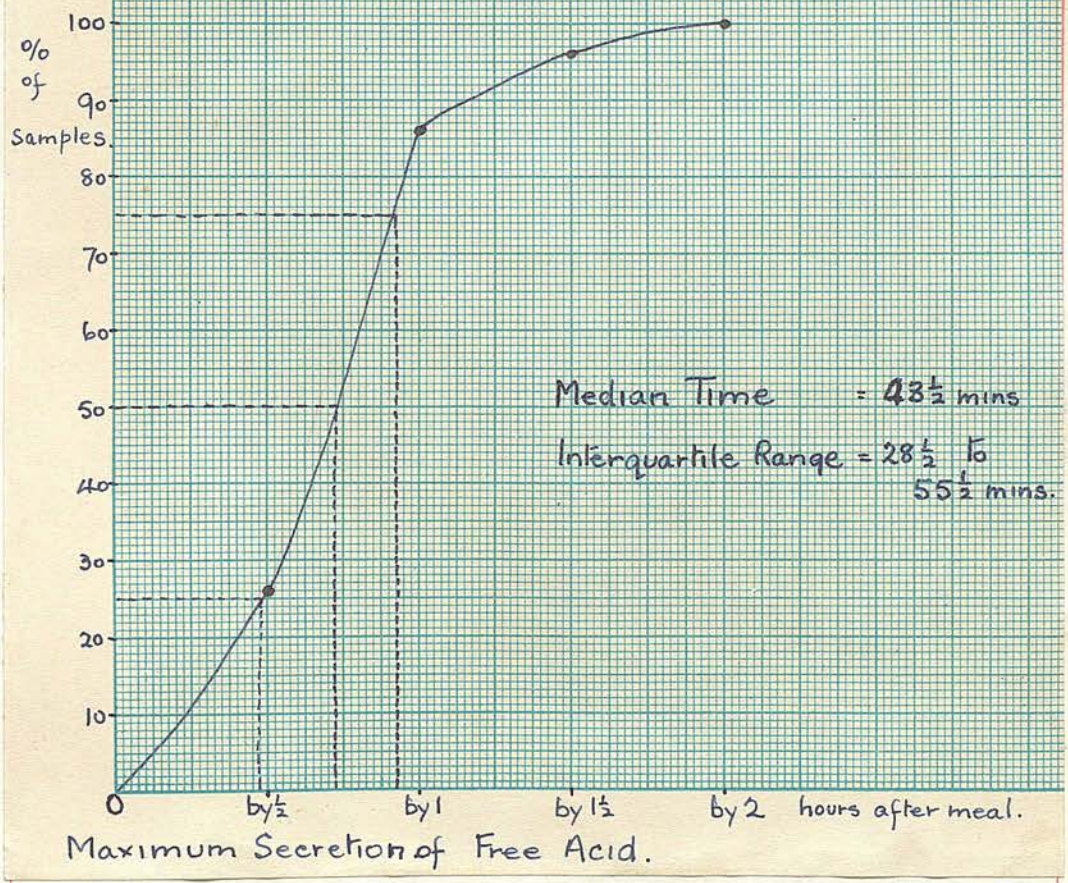
Footnote. A summary is given at the end of each section.


GRAPH I
GASTRIC ACIDITY
NORMAL INFANTS
= FREE ACID
= TOTAL ACID
ACID IN mN.
60
55
50
45
40
35
30
25
20
15
10
5
0
5
10
15
20
25
30
35
40
45
50
55
AGE IN WEEKS.

GRAPH II

TIME OF MAXIMUM SECRETION.

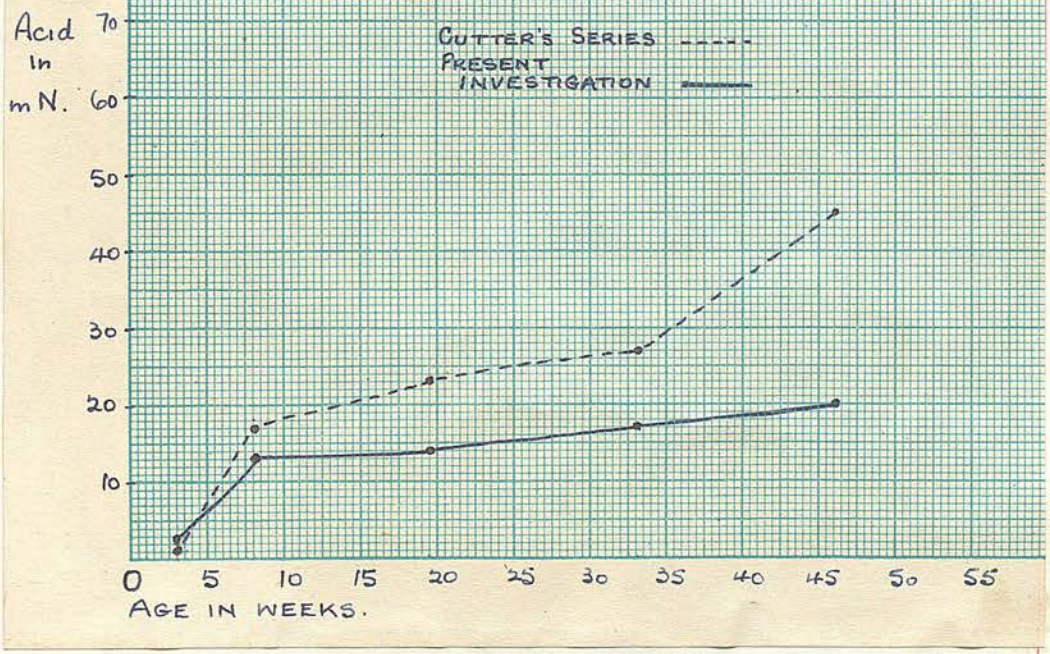
NORMAL.



Maximum Secretion of Free Acid.

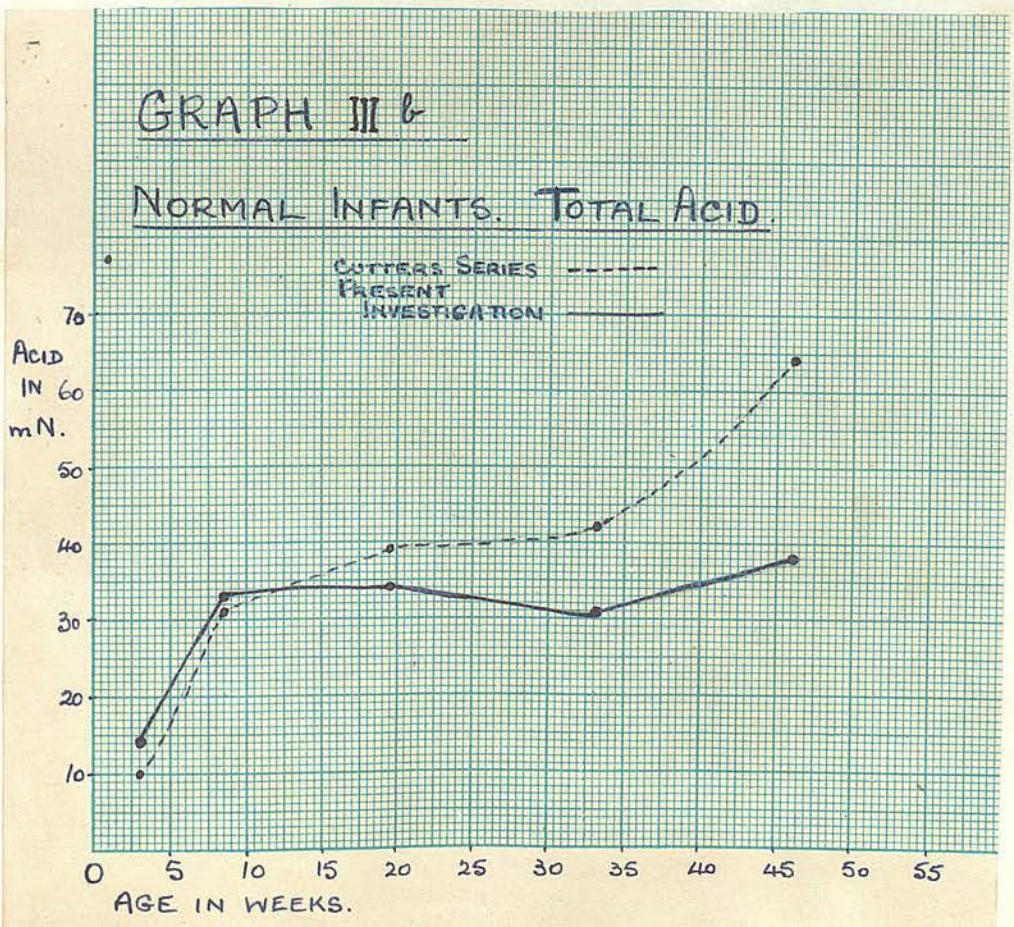
GRAPH III a

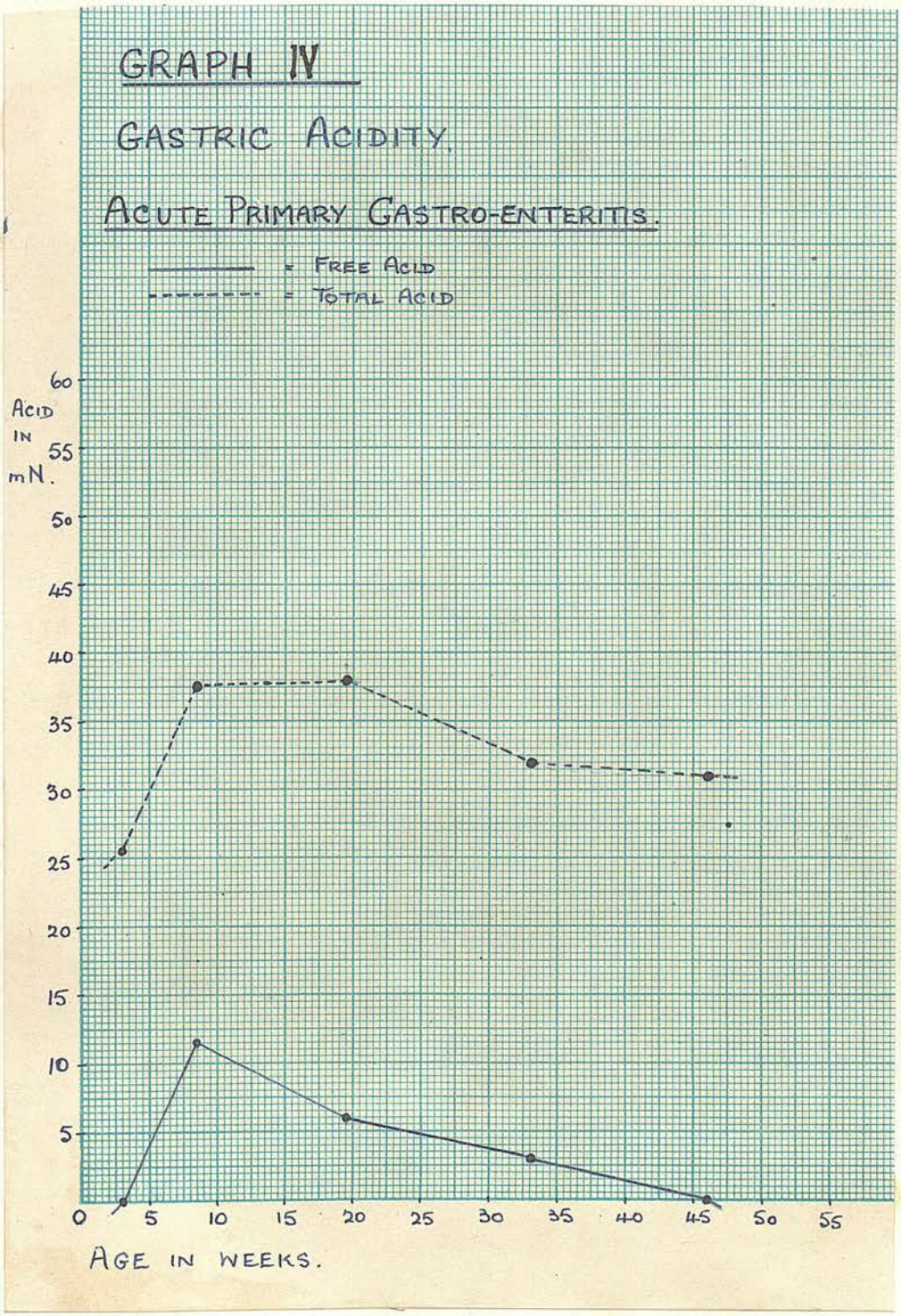
NORMAL INFANTS. FREE ACID

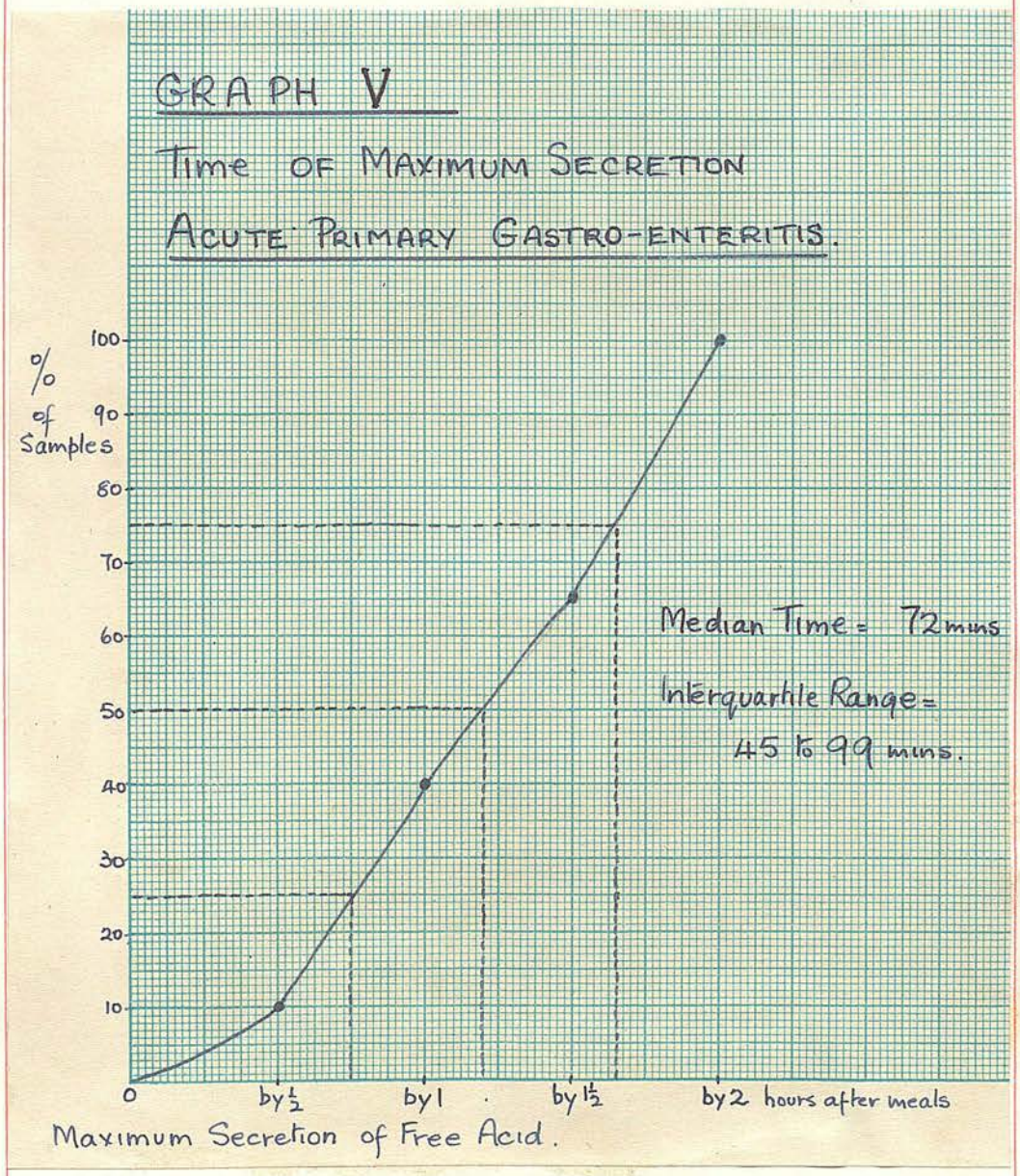


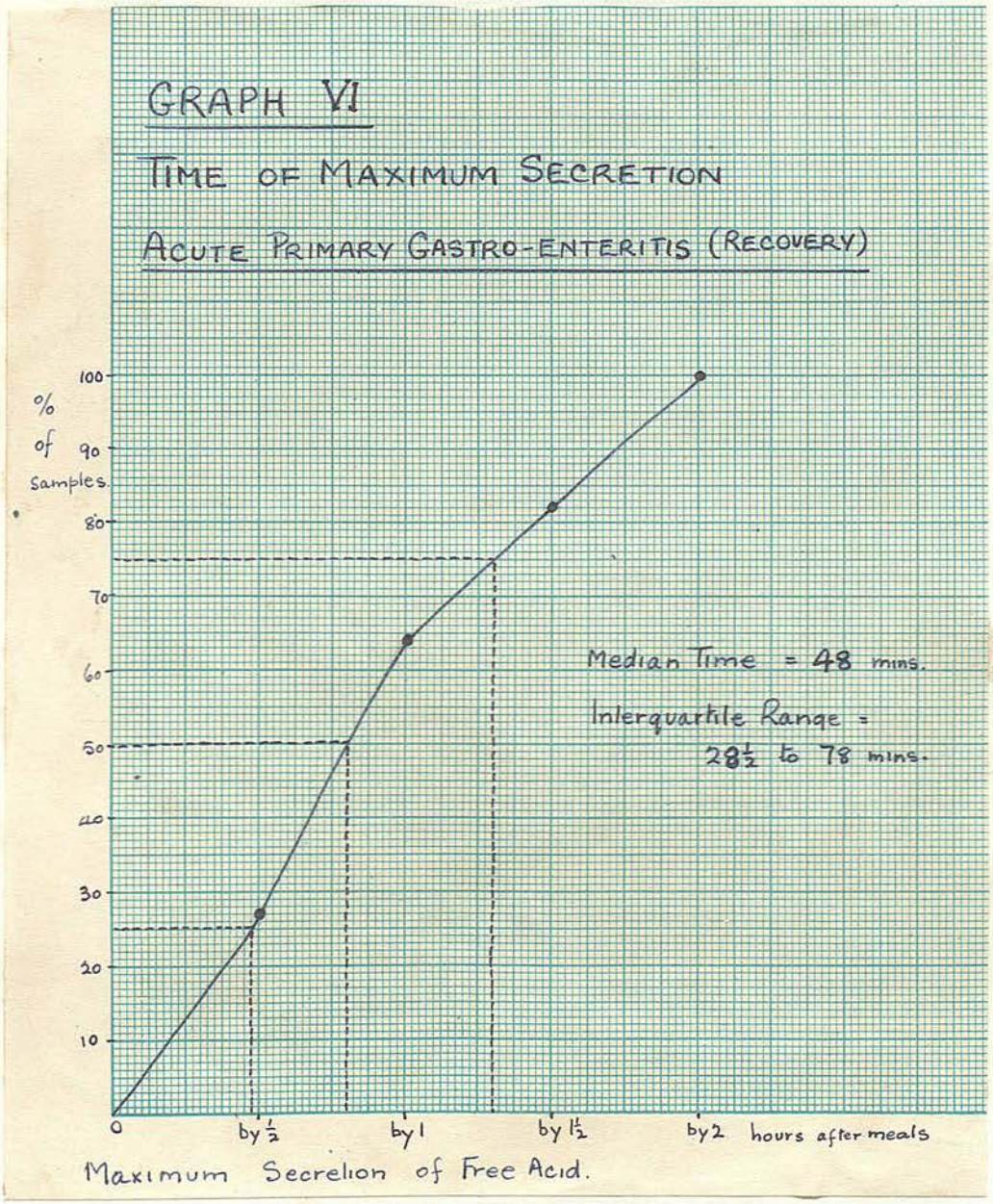
GRAPH III b

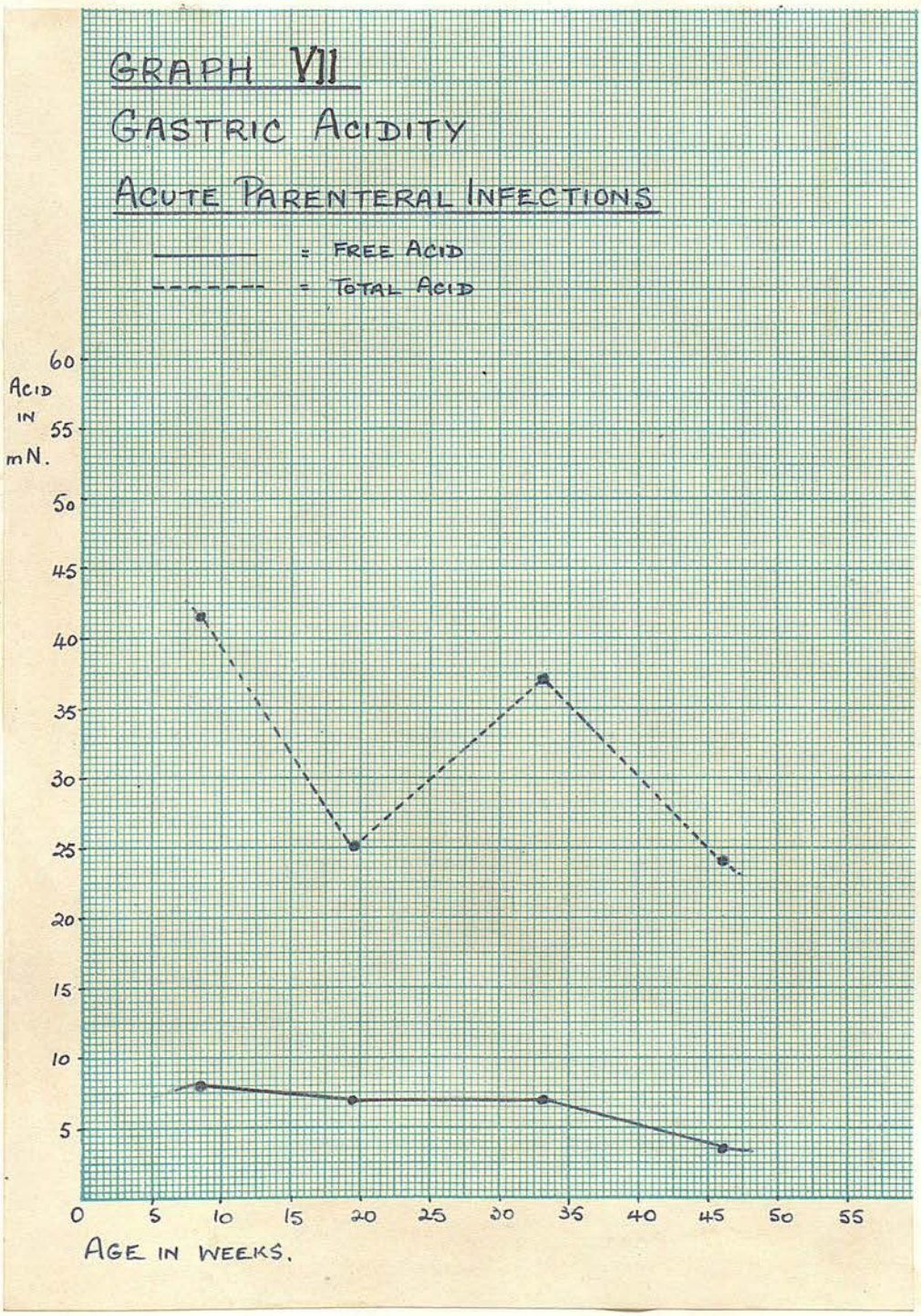
NORMAL INFANTS. TOTAL ACID.

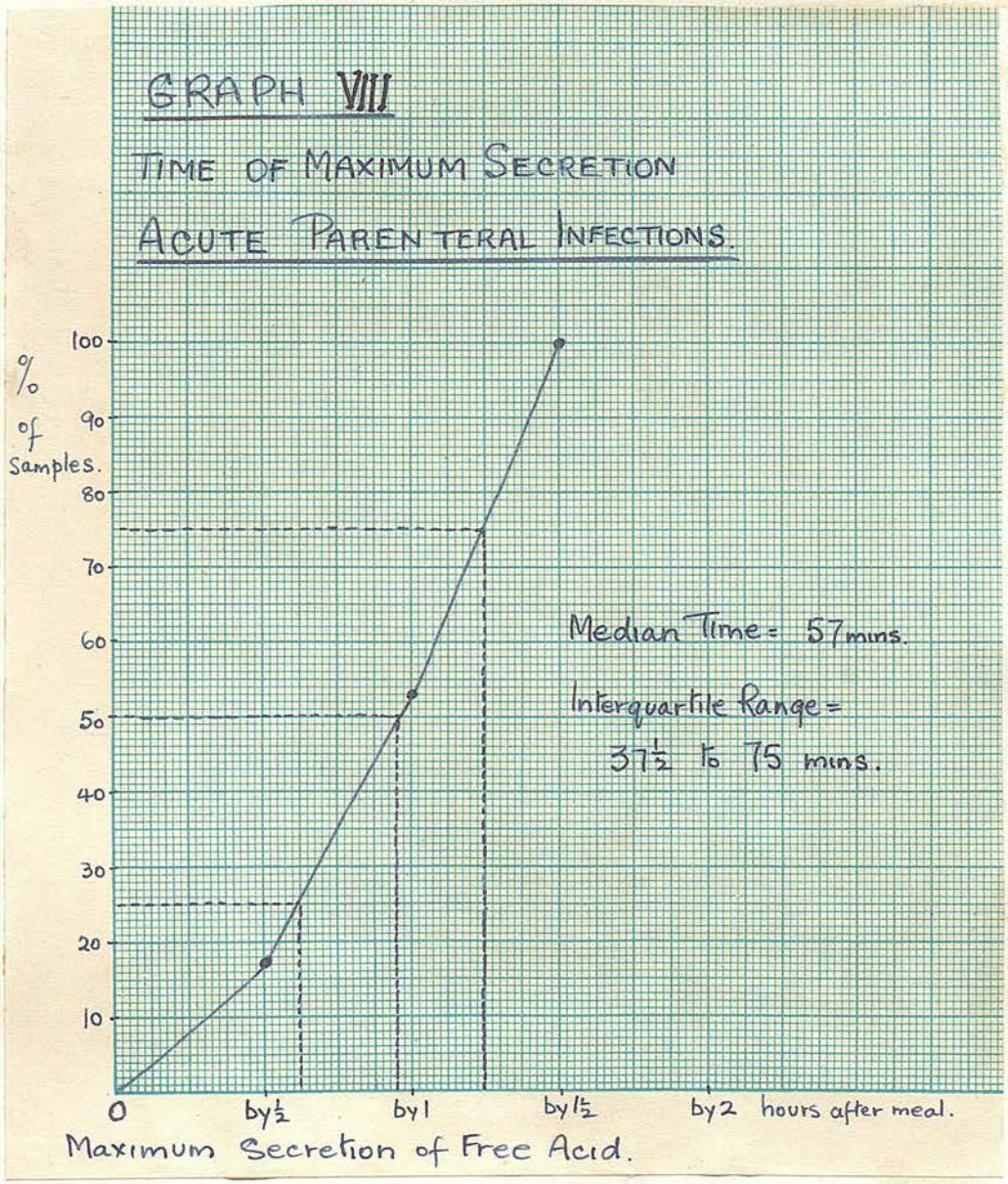


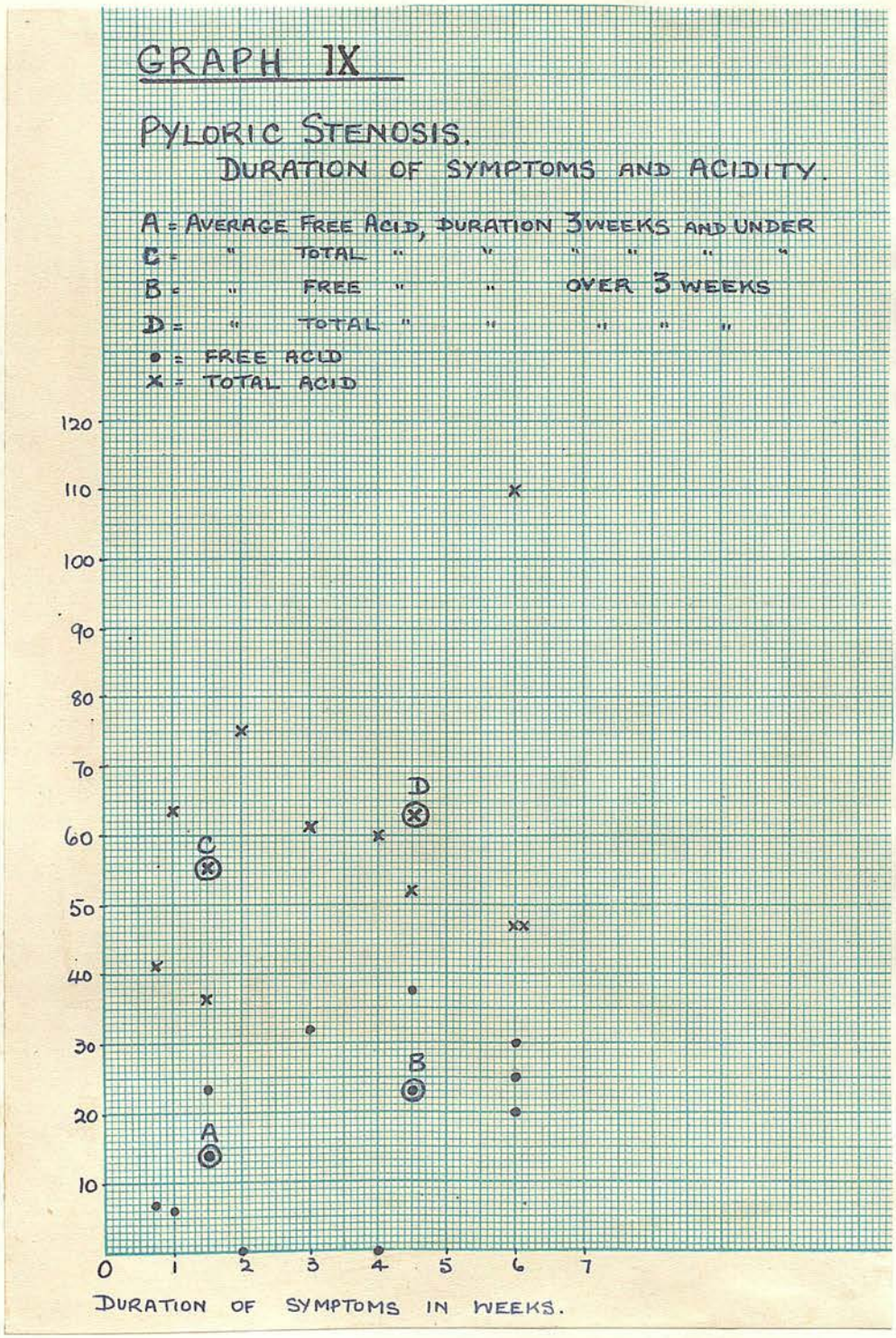

GRAPH IV
GASTRIC ACIDITY.
ACUTE PRIMARY GASTRO-ENTERITIS.
= FREE ACID
= TOTAL ACID
ACID IN mN.
60
55
50
45
40
35
30
25
20
15
10
5
0
5
10
15
20
25
30
35
40
45
50
55
AGE IN WEEKS.


GRAPH V
Time of Maximum Secretion
Acute Primary Gastro-enteritis.
% of Samples
100
90
80
70
60
50
40
30
20
10
0
by ½
by 1
by 1½
by 2 hours after meals
Median Time = 72 mins
Interquartile Range = 45 to 99 mins.
Maximum Secretion of Free Acid.


GRAPH VI
TIME OF MAXIMUM SECRETION
ACUTE PRIMARY GASTRO-ENTERITIS (RECOVERY)
% of Samples.
100
90
80
70
60
50
40
30
20
10
0
by ½
by 1
by 1½
by 2 hours after meals
Median Time = 48 mins.
Interquartile Range = 28½ to 78 mins.
Maximum Secretion of Free Acid.

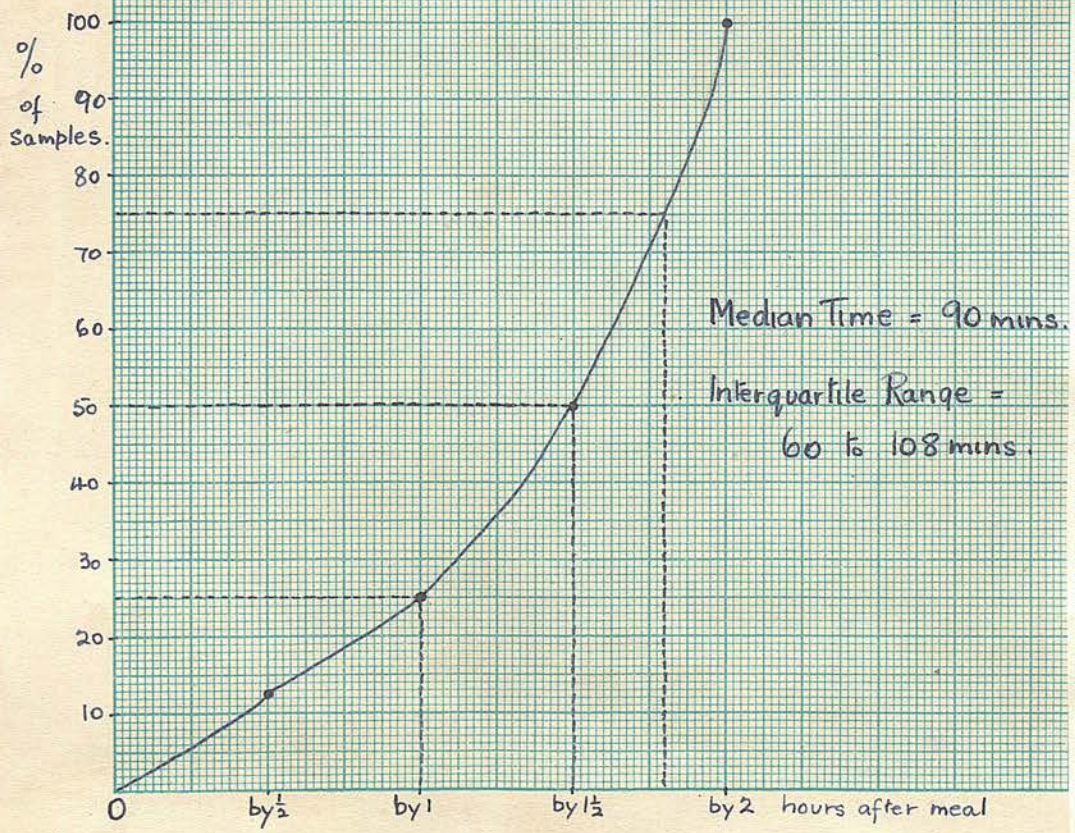

GRAPH VII
GASTRIC ACIDITY
ACUTE PARENTERAL INFECTIONS
= FREE ACID
= TOTAL ACID
ACID IN mN.
60
55
50
45
40
35
30
25
20
15
10
5
0
5
10
15
20
25
30
35
40
45
50
55
AGE IN WEEKS.


GRAPH VIII
TIME OF MAXIMUM SECRETION
ACUTE PARENTERAL INFECTIONS.
% of Samples.
100
90
80
70
60
50
40
30
20
10
Median Time = 57 mins.
Interquartile Range =
37½ to 75 mins.
0
by ½
by 1
by 1½
by 2 hours after meal.
Maximum Secretion of Free Acid.

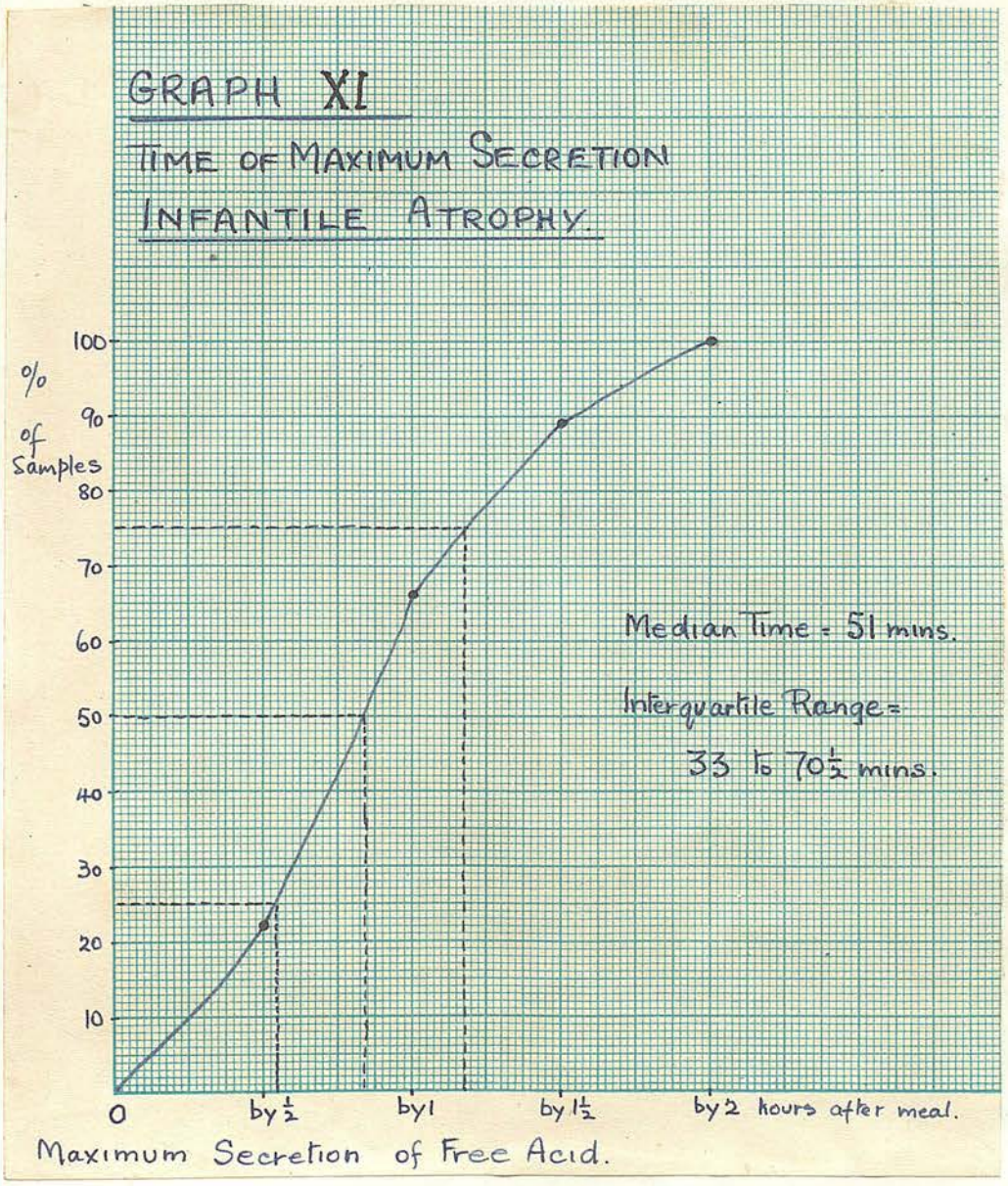

GRAPH IX
PYLORIC STENOSIS.
DURATION OF SYMPTOMS AND ACIDITY.
A = AVERAGE FREE ACID, DURATION 3 WEEKS AND UNDER
C = " TOTAL " " " " " " "
B = " FREE " " OVER 3 WEEKS
D = " TOTAL " " " " "
• = FREE ACID
× = TOTAL ACID
120
110
100
90
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
A
B
C
D
DURATION OF SYMPTOMS IN WEEKS.

GRAPH X

TIME OF MAXIMUM SECRETION PYLORIC STENOSIS.



Maximum Secretion of Free Acid.


GRAPH XI
TIME OF MAXIMUM SECRETION
INFANTILE ATROPHY.
% of Samples
100
90
80
70
60
50
40
30
20
10
0
by ½
by 1
by 1½
by 2 hours after meal.
Median Time = 51 mins.
Interquartile Range =
33 to 70½ mins.
Maximum Secretion of Free Acid.

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APPENDIX A.

In the tabulation of the results in all the appendices, the following plan has been followed :-

Upper line = free acid.
Lower line = total acid in each instance.
All values in m N.
A = amount of gastric contents sufficient only for qualitative test for free hydrochloric acid.
B = specimen discarded as bile stained.
+ = Free hydrochloric acid, qualitative test with Topfer's Reagent.
/ = Stomach empty.

Fractional Test Meal findings using gruel in Normal Infants.

Name.	Age in weeks.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hr.	2 hr.	Emptying Time.
1.G.C.	3	0 A	0 6.7	0 10.2	0 10.0	0 8.0	Over 2 hrs.
2.C.B.	3	0 6.0	2.5 9.0	4.0 21.5	0 A	/ /	1½ - 2 hrs.
3.-R.	3½	1.0 8.0	0 9.0	1.5 17.0	0 16.0	0 14.0	1½ - 2 hrs.
4.A.T.	3½	5.0 9.0	0 6.0	3.0 8.0	0 A	/ /	1 - 1½ hrs.
5.D.B.	6	+ A	0 26.0	5.0 44.0	1.8 27.5	+ A	1½ - 2 hrs.
6.F.R.	7	5.5 11.0	0 14.5	22.0 30.0	0 36.0	0 24.0	Over 2 hrs.
7.B.F.	7	0 A	21.0 36.0	20.0 27.0	9.0 12.5	/ /	1½ - 2 hrs.
8.A.W.	9	5.0 13.0	7.0 14.0	18.0 20.0	5.0 15.0	5.0 14.0	Over 2 hrs.
9.-B.	9	0 A	1.0 12.0	3.0 17.0	4.0 22.0	0 14.0	Over 2 hrs.
10.-M.	11	16.0 44.0	2.5 17.5	13.5 32.5	0 14.0	0 10.0	1- 1½ hrs.
11.A.W.	12	2.0 8.0	0 13.0	4.0 38.0	0 B	0 B	Over 2 hrs.
12.-McL.	12	8.0 28.0	2.0 20.0	15.5 35.5	0 16.0	0 9.5	1½ - 2 hrs.

Name.	Age in weeks.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.
13. -B.	13	0 A	1.0 26.0	8.0 30.2	1.0 30.0	0 25.0	Over 2 hrs.
14. R. W.	16	10.0 30.0	10.0 14.0	13.5 21.8	15.0 31.0	19.5 42.0	Over 2 hrs.
15. - H.	18	2.0 9.5	0 7.4	6.5 16.5	14.8 34.5	8.5 18.0	Over 2 hrs.
16. A. T.	20	0 36.0	14.0 29.0	7.0 17.0	0 9.0	0 8.0	1 - 1½ hrs.
17. A. H.	22	5.0 18.0	16.0 33.0	6.0 16.5	0 15.0	0 6.0	Over 2 hrs.
18. M. B.	28	0 10.0	13.2 25.5	0 17.5	0 6.0	0 4.0	Over 2 hrs.
19. -W.	28	0 28.0	11.0 32.0	19.0 36.0	0 33.0	0 20.0	Over 2 hrs.
20. -A.	35	+ A	6.0 15.5	18.5 32.0	10.0 30.0	0 24.0	Over 2 hrs.
21. B. G.	40	12.0 32.0	3.0 20.0	19.0 33.0	12.0. 27.0	4.5 12.5	Over 2 hrs.
22. -M.	42	+ A	17.4 28.0	6.5 20.0	0 14.0	0 7.5	Over 2 hrs.
23. -R.	45	6.4 20.0	20.0 40.0	10.0 28.0	4.5 26.0	3.0 12.0	Over 2 hrs.
24. A. B.	48	2.0 6.0	5.0 18.0	23.0 50.0	23.0 50.0	0 32.5	Over 2 hrs.

APPENDIX B.

Table I. Fractional test meal findings using gruel in infants under 1 year suffering from acute gastro-enteritis.

+++ = severely ill.
++ = moderately ill.
+ = mildly ill.
F = temperature of 100°F. sometime during the 24 hours before test meal is given.

Name.	Age in wks.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.	Severity of illness, & fever
1.E.D.	3	0 75.0	0 12.5	0 17.5	0 23.0	0 6.0	Over 2 hrs.	++ F.
2.S.D.	4	0 21.0	0 28.0	0 20.5	0 A	/ /	1 -1½ hrs.	++
3.M.H.	5	0 A	0 19.0	0 29.0	0 47.0	0 18.0	1½-2 hrs.	+++
4.W.S.	5	0 A	0 27.0	0 36.0	0 25.0	0 8.0	1½-2 hrs.	++
5.S.B.	6	4.0 57.0	0 12.0	14.0 38.0	8.0 21.0	0 17.0	1½-2 hrs.	+++
6.P.F.	6	0 15.0	3.0 20.0	0 18.0	0 16.5	0 15.0	1½-2 hrs.	++
7.J.G.	6	0 43.5	8.0 28.0	9.5 28.5	0 17.5	0 25.0	Over 2 hrs.	++ F.
8.C.H.	6	0 17.0	0 16.5	0 35.0	0 66.0	0 30.0	1½-2 hrs.	+++
9.W.J.	7	0 A	0 16.0	0 13.0	0 12.0	0 A	1-1½ hrs.	++ F.
10.I.R.	8	/ /	0 21.0	20.5 45.0	11.0 28.0	3.5 9.5	Over 2 hrs.	++ F.
11.J.M.	8	0 30.0	7.0 13.0	12.5 32.0	17.0 39.0	9.0 35.0	1½-2 hrs.	+ F.
12.T.G.	9	0 37.4	0 5.0	0 12.0	0 20.0	0 23.0	Over 2 hrs.	+++
13.A.B.	9	0 13.0	0 8.0	0 14.0	0 19.5	0 17.0	1-1½ hrs.	+++ F.
14.C.C.	10	0 33.0	0 7.0	0 7.0	0 18.0	0 12.0	Over 2 hrs.	++ F.

Name.	Age in wks.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.	Severity of illness, & fever.
15. N. G.	10	0 10.5	0 9.5	2.0 15.5	20.5 39.5	33.0 51.0	Over 2 hrs.	+ F.
16. T. C.	11	0 20.0	11.0 23.5	28.5 50.5	40.0 72.0	17.0 66.5	Over 2 hrs.	++
17. M. K.	12	0 32.5	11.0 28.0	6.0 26.0	35.0 55.0	39.0 61.0	Over 2 hrs.	+
18. C. K.	12	0 A	0 12.5	0 13.0	0 13.0	6.0 25.0	1½-2 hrs.	+ F.
19. S. C.	13	0 25.0	0 10.0	0 12.0	0 14.0	5.0 22.0	Over 2 hrs.	+++
20. M. C.	13	0 33.0	0 9.0	0 10.0	0 10.0	0 12.0	Over 2 hrs.	+
21. C. L.	15	0 12.0	0 9.0	0 10.0	0 12.0	0 10.0	Over 2 hrs.	+ F.
22. H. F.	16	0 A	0 9.0	0 46.0	0 40.0	0 A	1-1½ hrs.	+++
23. M. G.	16	0 20.5	0 5.5	0 7.0	0 11.0	7.5 19.0	1-1½ hrs.	+ F.
24. R. P.	16	0 22.0	3.5 50.0	48.0 89.0	23.0 53.5	0 9.0	Over 2 hrs.	+ F.
25. M. R.	16	0 8.0	0 6.0	0 37.0	0 12.5	0 10.0	Over 2 hrs.	+++F.
26. D. S.	16	/ /	0 6.0	21.2 51.0	25.5 54.0	0 5.0	Over 2 hrs.	+++
27. L. D.	17	0 A	0 11.0	0 24.5	0 39.0	0 22.0	Over 2 hrs.	+++
28. J. C.	17	0 14.5	0 31.0	0 42.0	0 15.0	0 A	1-1½ hrs.	+++
29. M. G.	18	0 38.0	0 35.0	0 36.5	0 52.0	0 79.0	1-1½ hrs.	+++
30. A. S.	18	0 82.0	0 23.0	0 31.5	0 73.0	0 81.0	Over 2 hrs.	+++
31. H. G.	18	0 22.0	0 16.0	0 18.0	0 20.0	0 22.0	Over 2 hrs.	+++ F.
32. M. M. A	19	0 31.0	0 26.5	3.0 39.0	0 30.0	/ /	1-1½ hrs.	+++
33. R. R.	19	0 36.5	0 16.0	0 32.0	0 41.0	0 40.0	Over 2 hrs.	++

Name.	Age in wks.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.	Severity of illness, & fever.
34. P.K.	21	0 35.0	0 6.0	0 13.0	0 27.0	6.0 29.0	Over 2 hrs.	+ F.
35. D.D.	21	0 26.0	0 18.0	0 39.0	0 16.0	0 12.0	1-1½ hrs.	++
36. R.L.	22	0 A	0 4.0	0 5.0	0 9.0	0 10.0	Over 2 hrs.	+
37. E.K.	23	0 8.0	8.0 29.0	5.0 27.0	0 7.0	0 6.0	Over 2 hrs.	+ F.
38. I.N.	23	22.0 52.0	0 23.0	0 15.0	26.5 42.5	26.0 41.5	Over 2 hrs.	+ F.
39. J.H.	26	0 A	0 6.5	0 7.0	0 6.0	0 4.0	1½-2 hrs.	+++
40. F.H.	26	0 20.5	0 6.0	0 19.0	10.0 24.0	6.5 21.0	Over 2 hrs.	++ F.
41. H.M.	26	0 A	0 28.0	0 70.0	0 35.5	0 18.0	Over 2 hrs.	+++
42. A.M.	26	0 A	0 32.0	0 24.0	0 16.0	0 12.0	1½-2 hrs.	++
43. R.M.G	27	0 17.0	5.5 30.5	10.5 46.0	0 37.0	0 22.0	Over 2 hrs.	++
44. E.L.	28	0 A	0 3.5	0 7.0	0 9.9	7.0 28.0	Over 2 hrs.	+
45. J.F.	32	0 32.0	0 14.5	0 29.5	0 35.0	0 45.0	Over 2 hrs.	+ F.
46. J.S.	34	0 20.0	0 12.0	0 18.0	0 18.0	0 24.0	Over 2 hrs.	+++ F.
47. A.S.	34	0 24.5	0 30.0	0 24.5	0 17.0	0 10.0	1½-2 hrs.	+ F.
48. H.M.	36	0 47.0	0 17.0	0 11.0	0 3.0	0 A	1½-2 hrs.	+++
49. A.S.	44	0 10.0	0 22.0	0 9.0	0 7.0	0 7.0	Over 2 hrs.	++
50. M.T.	48	0 22.0	0 14.5	0 25.0	0 15.0	0 3.0	½-1 hr.	+
51. J.B.	49	0 A	0 38.0	0 45.0	0 42.0	0 40.0	Over 2 hrs.	++

Table 2. Acute primary gastro-enteritis.

Fractional test meal using combined gruel and histamine stimulus.

Name.	Fasting Juice.	Fractional test meal. ½ hr.	1hr.	1½ hrs.	2 hrs.	Emptying Time.
1.E.D.	0 37.0	0 12.5	0 16.5	0 24.0	6.5 28.0	Over 2 hrs.
4.J.S.	0 6.5	4.0 24.0	0 41.0	0 64.0	0 71.0	Over 2 hrs.
8.C.H.	0 15.0	6.0 28.0	0 42.5	0 66.0	B B	Over 2 hrs.
12.T.G.	0 27.0	0 12.0	0 43.0	10.0 44.0	0 31.0	Over 2 hrs.
13.A.B.	0 23.5	2.5 15.0	3.0 20.5	1.5 12.0	0 8.5	Over 2 hrs.
14.C.C.	0 44.0	0 16.0	8.0 29.0	11.0 55.0	10.0 36.0	Over 2 hrs.
20.M.C.	0 A	0 16.0	0 29.0	7.0 45.0	0 4.0	Over 2 hrs.
21.C.L.	0 14.0	0 8.0	0 8.0	0 13.0	0 14.0	Over 2 hrs.
22.H.F.	0 10.0	5.0 28.6	5.0 22.0	0 18.0	0 13.0	Over 2 hrs.
29.M.G.	0 A	14.0 39.0	0 35.0	0 26.0	0 20.0	Over 2 hrs.
30.A.S.	0 88.0	5.0 54.0	0 62.0	0 72.0	0 81.0	Over 2 hrs.
31.H.G.	0 28.0	0 12.0	7.0 33.0	0 24.0	0 22.0	Over 2 hrs.
33.R.R.	0 18.5	3.0 41.0	20.5 55.0	0 39.0	0 A	1½-2 hrs.
39.J.H.	0 A	0 6.0	0 6.0	0 3.5	0 A	½-1 hr.
41.H.M.	0 A	2.0 28.0	10.0 31.0	10.0 29.0	8.5 25.0	Over 2 hrs.
42.A.M.	0 A	0 19.0	0 32.0	5.5 52.0	0 50.0	1½-2 hrs.
49.A.S.	0 20.0	0 9.0	12.0 20.0	0 10.0	0 6.0	1-1½ hrs.
50.M.T.	0 30.5	0 15.0	0 16.0	0 23.0	0 9.0	1½-2 hrs.

Table 3.

Acute primary gastro-enteritis. Fractional test meal of gruel during relapse.

Name	Fasting Juice	Fractional test meal				Emptying Time
		½ hr.	1 hr.	1½ hrs.	2 hrs.	
12.T.G.	0 A.	0 12.0	0 34.0	0 54.0	0 40.5	1½ - 2 hrs.
14.C.C.	0 42.0	0 28.0	0 15.0	0 5.0	0 5.0	Over 2 hrs.

Table 4.

Fractional test meal of gruel given during parenteral infection, some weeks after acute primary gastro-enteritis.

Name	Interval after 1st test meal	Fasting Juice	Fractional Test Meal				Emptying time
			½ hr.	1 hr.	1½ hrs.	2 hrs.	
1.E.D.	8wks.	0 20.0	0 13.5	0 14.0	0 22.0	0 11.0	Over 2 hrs.
1 E.D.	17 wks.	25.0 91.5	0 9.0	0 9.0	0 10.0	0 19.0	Over 2 hrs.
48 H.M.	16 wks.	0 21.5	0 40.5	20.0 47.0	12.0 39.0	2.5 13.0	Over 2 hrs.

Table 5. Acute primary gastro-enteritis.

Fractional test meal of gruel during convalescence and recovery.

Name	Interval after 1st test meal in days.	Fasting Juice	Fractional Test Meal ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.
1. E. D.	27	0 44.0	0 43.0	8.0 50.0	6.0 35.0	A A	Over 2 hrs.
2. S. D.	21	0 13.0	0 31.5	14.0 61.5	6.0 29.0	5.0 23.0	Over 2 hrs.
15. N. G.	55	25.0 62.0	0 46.0	0 28.0	0 21.0	0 14.0	Over 2 hrs.
17. M. K.	59	7.0 69.0	0 30.0	0 84.0	0 40.0	0 38.0	Over 2 hrs.
21. C. L.	45	28.0 88.0	0 10.0	0 25.0	0 27.0	0 31.0	Over 2 hrs.
26. D. S.	26	12.5 44.5	0 17.0	15.0 55.0	15.0 54.0	10.0 28.5	1½-2 hrs.
28. J. C.	25	21.0 58.0	3.0 35.0	0 25.0	0 19.0	0 19.0	1-1½ hrs.
32. M. M.	26	0 44.0	9.0 28.0	9.0 24.0	0.0 20.0	0 A	Over 2 hrs.
36. R. L.	36	4.0 14.0	5.0 35.0	2.0 25.0	0 14.0	0 12.0	Over 2 hrs.
41. H. M.	32	0 125.0	3.0 55.0	0 18.0	10.0 49.0	32.0 63.0	Over 2 hrs.
42. A. M.	8	0 69.0	0 18.5	0 19.0	0 34.0	2.0 20.0	1½-2 hrs.
42. A. M.	32	/ /	0 59.0	11.0 66.0	6.0 34.0	0 20.0	1-1½ hrs.
43. R. M.	8	/	2.0 19.0	5.5 62.0	28.0 81.0	B. B.	1½-2 hrs.
44. E. L.	51	0 8.0	0 36.0	0 40.0	12.0 83.0	/ /	1-1½ hrs.
48. H. M.	36	7.0 56.0	0 21.6	0 37.0	0 27.0	0 25.0	Over 2 hrs.

APPENDIX C.

TABLE 1. Fractional Test Meal findings using gruel in infants under 1 year, suffering from acute parenteral infection.

D = Diarrhoea.
V = Vomiting.
F = Temperature of 100° F. sometime during 24 hours before test meal given.

Name.	Age in weeks.	Fasting Juice.	Fractional Test Meal. ½ hr.	1 hr.	1½ hr.	2hr.	Emptying Time.	D.V.F
1.C.C.	5	0 13.5	0 45.0	0 16.0	0 15.0	0 10.0	1½ - 2hrs.	D.V.F
2.R.B.	6	0 52.0	0 17.5	10.0 35.5	33.0 53.0	0 29.0	Over 2 hrs.	D.V.F
3.J.T.	6	0 56.5	0 74.0	0 70.0	0 51.5	0 37.5	Over 2 hrs.	
4.G.H.	7	1.0 15.0	10.0 18.0	21.0 30.0	0 18.0	0 13.0	1 - 1½ hrs.	D.V.
5.S.H.	8	0 44.0	0 18.0	0 42.0	0 15.0	0 11.5	Over 2 hrs.	D.
6.R.McN.	8	0 8.0	0 7.5	0 17.0	0 12.0	0 3.0	Over 2 hrs	D. F.
7.D.C.	9	3.0 35.0	0 13.5	5.0 25.0	3.0 13.0	4.0 23.0	1½ - 2 hrs.	D.
8.R.L.	9	0 A	6.5 41.0	0 42.0	0 35.0	0 19.0	Over 2 hrs.	F.
9.S.R.	11	2.0 18.5	0 18.0	0 19.5	10.0 49.5	0 9.5	1 - 1½ hrs.	
10.R.M.	13	0 A	0 17.0	4.5 30.0	26.0 43.0	21.0 33.0	Over 2 hrs	D.V.F
11.J.M.	15	0 36.0	0 20.0	6.0 32.0	0 32.0	0 26.0	Over 2hrs.	F.
12.A.S.	15	0 33.5	0 13.0	5.0 24.0	5.0 22.0	4.0 10.0	1½ - 2 hrs	V.F.
13.S.F.	15	0 A	0 23.5	5.5 31.5	4.0 25.5	3.0 13.5	Over 2 hrs	
14.G.M.	18	0 3.5	0 11.5	0 7.5	0 5.0	0 A	1 - 1½ hrs	D.V.F
15.H.A.	22	0 26.5	0 11.0	0 9.0	0 8.0	0 8.0	1 - 1½ hrs.	F.
16.F.S.	23	0 10.0	0 2.0	0 9.0	4.0 20.0	0 14.5	Over 2 hrs	D. F.

Name.	Age in weeks.	Fasting Juice.	Fractional Test Meal. ½ hr.	1 hr.	1½ hr.	2 hr.	Emptying Time.	D.V.F.
17.R.R.	26	0 A	10.0 27.0	0 17.0	0 13.0	0 13.0	½ - 1 hr.	F
18.M.C.	30	0 9.8	0 13.0	0 18.5	16.0 58.0	16.0 49.5	Over 2 hrs.	D.
19.P.H.	30	- -	0 20.0	0 26.0	0 34.0	0 41.0	1½ - 2 hrs.	
20.J.McC.	31	0 17.0	0 28.0	0 25.0	0 19.0	0 10.0	Over 2 hrs.	F
21.T.K.	32	0 3.0	0 4.0	0 5.0	0 8.5	0 11.0	Over 2 hrs.	D.V.F.
22.D.K.	34	0 3.0	6.5 25.0	5.5 25.0	0 12.0	6.0 20.0	1½ - 2 hrs.	D.
23.R.B.	36	0 13.0	0 28.5	2.5 35.5	7.0 54.0	5.5 15.0	1½ - 2 hrs.	
24.C.H.	38	0 A	0 24.0	7.5 40.5	18.0 49.5	0 21.0	Over 2 hrs.	V.F.
25.D.C.	38	0 71.5	0 15.0	6.0 22.0	8.5 31.0	5.0 11.0	1½ - 2 hrs.	
26.P.K.	40	18.0 64.0	6.5 27.5	7.0 32.0	0 6.0	B B	Over 2 hrs.	D. F.
27.R.M.	47	0 A	0 4.0	0 8.0	0 16.0	0 14.5	1½ - 2 hrs.	D.V.F.

TABLE 2. Acute parenteral infection. Fractional test meal using combined histamine and gruel stimulus.

Name.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hr.	2 hr.	Emptying Time.
3.J.T.	0 41.0	0 31.0	10.0 85.0	8.5 57.5	0 35.0	Over 2 hrs.
14.G.M.	0 A	0 9.0	0 12.0	0 9.0	0 8.5	Over 2 hrs.
19.P.H.	0 A	12.0 30.0	15.0 55.0	2.0 35.5	0 21.0	Over 2 hrs.
21.T.K.	0 16.0	0 23.0	6.0 26.0	10.0 36.0	0 9	1½ - 2 hrs.
27.R.M.	0 13.5	3.0 24.5	9.5 30.0	0 25.0	B B	1½ - 2 hrs.

Table 3. Acute parenteral infections.

Fractional test meal of gruel later in the disease, and in recovery.

Name.	Interval after 1st. test meal.	Fasting Juice.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.
20. J. M. C	10 days.	0 A	0 25.0	0 18.0	0 13.0	0 8.0	Over 2 hrs.
	6 weeks.	3.0 33.0	0 23.0	9.0 37.0	14.0 43.5	0 20.0	Over 2 hrs.
22. D. K.	11 days	0 18.0	0 5.0	0 12.0	0 12.0	0 10.0	1½-2 hrs.
	5 weeks.	0 8.0	0 12.5	9.5 21.5	7.0 18.0	0 3.0	1½-2 hrs.

APPENDIX D.

Table 1. Fractional test meal findings using gruel in infants with pyloric stenosis.

Name.	Age in wks.	Fasting juice. Amount in ccs.	Fasting juice. Acidity mN.	Fractional test meal. ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.
1. J.B.	3	20	20.5 98.0	0 7.5	0 11.0	0 30.0	23.5 36.5	Over 2 hrs
2. R.M.C.	4	22	0 72.5	0 45.0	0 61.0	6.0 63.5	0 57.5	Over 2 hrs
3. D.B.	4	25	0 10.0	0 26.0	7.0 27.0	5.0 30.0	4.5 41.5	Over 2 hrs
4. R.S.	5	4	0 32.5	0 18.0	0 75.0	0 40.0	0 22.0	Over 2 hrs
5. A.M.X	6	15	1.0 97.0	0 10.0	11.0 35.0	20.0 45.0	25.0 47.0	Over 2 hrs
6. T.S.	8	6	0 103.5	20.5 102.0	16.0 110.0	14.0 71.5	12.0 62.0	Over 2 hrs.
7. W.C.	8	40	0 12.4	10.0 36.0	14.0 43.0	30.0 47.0	24.0 39.0	Over 2 hrs
8. T.D.	8	15	0 110.0	0 44.0	0 60.0	0 50.0	0 44.0	1½-2 hrs.
9. J.M.N	8	27	29.0 77.5	0 20.5	14.0 38.5	27.5 49.0	32.0 61.5	Over 2 hrs
10. J.H.	12	30	31.5 104.0	3.0 22.0	21.0 37.0	28.0 40.0	38.5 52.5	Over 2 hrs

Table 2. Repeat fractional test meals in infants with pyloric stenosis.

Name.	Interval after 1st. test meal.	Method of examn.	Fasting Juice.	Fractional test meal ½ hr.	1 hr.	1½ hrs.	2 hrs.	Emptying Time.
4. R.S.	7 weeks.	Gruel.	0 38.5	0 24.0	0 35.0	0 35.0	6.0 48.0	Over 2 hrs
6. T.S.	1½ weeks.	Gruel.	10.0 57.0	0 20.0	2.0 25.0	31.0 47.0	60.0 76.0	Over 2 hrs.
8. T.D.	1 day.	Gruel and Histamine.	0 93.0	0 65.0	0 35.5	0 25.0	0 22.5	1½-2 hrs.

APPENDIX E

(A) In the Infantile Atrophy group, in estimating the percentage under normal weight, a normal child was taken as weighing 3.20 kilo at birth, and as gaining weight at the rate of 0.15 kilo. per week.

Table 1. Fractional test meal findings in Infantile Atrophy.

Name	Age in weeks	Fasting Juice	Fractional test meal				Emptying Time
			½ hr.	1 hr.	1½hr.	2hrs.	
1.J.L.	5	4.0 12.5	12.0 29.0	0 18.0	0 16.0	0 3.0	Over 2 hrs.
2.E.P.	5	0 72.0	0 15.0	0 53.0	20.0 69.0	18.0 52.0	Over 2 hrs.
3.E.C.	7	0 A	0 16.5	0 16.0	16.0 28.0	0 9.5	Over 2 hrs.
4.R.S.	8	0 45.0	0 42.0	0 12.5	0 12.0	0 11.0	1½-2 hrs
5.E.W.	8	17.0 57.0	26.0 76.0	26.0 59.0	25.0 44.0	18.0 27.0	0-½ hr.
6.S.McT.	9	32.5 66.5	0 14.0	19.0 36.0	18.0 35.0	18.0 35.0	Over 2 hrs.
7.C.McK.	10	0 16.0	0 36.5	11.3 39.5	0 25	B B	Over 2 hrs.
8.J.D.	14	0 24.0	21.0 39.0	45.0 57.5	45.0 56.0	21.0 27.5	1½-2 hrs
9.J.R.	15	0 A	13.0 26.0	0 21.0	5.5 15.0	19.5 41.5	Over 2 hrs.
10.J.H.	16	0 60.0	0 14.0	14.0 30.0	0 23.5	0 16.0	1½-2 hrs.

(B) Summary of case histories.

1.J.L. Aged 5 weeks. Second child. Normal confinement. Healthy at birth, weighed 6 lbs. Breast fed for 10 days, then put on to cows milk. At 1 month, the feed was altered to Ostermilk No.1. The child has never thriven. No vomiting. Stools normal.

2.E.P. Age 5 weeks. Fifth child. Normal confinement. Healthy at birth, weighed 6½ lbs. From the beginning, the baby was fed on National Dried Milk, full cream, according to the directions on the tin, but has never taken feeds well. For the week before admission, there was vomiting after feeds and frequent loose stools. There has been persistent loss of weight.

3.E.C. Aged 7 weeks. Second child. Normal confinement. Jaundiced shortly after birth, but otherwise healthy, weighed 6 lbs. 15 ozs. Fed on cows milk from birth. Appetite good, but the baby has vomited up all feeds since birth. Stools normal. The child has never thriven.

4.R.S. Aged 8 weeks. Second child. Normal confinement. Healthy at birth, weighed 7 lbs. Breast fed for 1 month, then put on to Ostermilk. The infant had intermittent vomiting from the age of 5 weeks; 3 days before admission, the feed was changed to cows milk, as the vomiting had become more frequent. Occasional green stools. Losing weight persistently since birth.

5.E.W. Aged 8 weeks. Fourth child. Normal confinement. Healthy at birth, weighed 7 lbs. Breast fed for 6 weeks, since when the baby has had National Dried Milk, full cream. She has vomited after most feeds since birth and has been constipated. The weight has been stationary for some time.

6.S.McT. Aged 9 weeks. Fifth child. Normal confinement. Healthy at birth, weighed ? lbs. Breast fed

for 6 weeks, since when given feeds of 2 ounces of cows milk with 2 ounces of water, 4 hourly. The infant has vomited at least one feed a day since birth. Bowels constipated. Has never thriven.

7.C.McK. Aged 10 weeks. Fourth child. Normal confinement. Healthy at birth, weighed ? lbs. Breast fed with complementary feeds of National Dried Milk, full cream, until 7 weeks of age, when the feed was changed to Robinson's Patent Barley and cows milk only. Diarrhoea and vomiting began 3 days before admission. There has been persistent loss of weight.

8.J.D. Aged 14 weeks. Third pregnancy, the child is one of twins. Breech delivery. Healthy at birth, weighed 5¾ lbs. Breast fed for 3 weeks, then given Cow and Gate, half cream. Septic spots for 1 week prior to admission. Loose stools for 2 days and vomiting for 1 day before admission to hospital. Has never gained weight satisfactorily.

9.J.R. Aged 15 weeks. Second child. Normal confinement. Healthy at birth, weighed 8 lbs. 2 ozs. Breast fed for 2 weeks, then changed to Ostermilk No.1 The infant vomited on this feed, so after 1 week it was given Sister Laura's Food. Whilst on this, there was occasional vomiting and frequent loose green stools, so the feed was again changed to National Dried Milk, full cream. The stools were unchanged, but the vomiting was less frequent. The baby has never thriven.

10.J.H. Aged 16 weeks. Third child. Normal confinement. Healthy at birth, weighed 11 lbs. Breast fed for 2 weeks, then put on to National Dried Milk, half cream; this was changed to full cream at 10 weeks. The infant had Acute Gastro-enteritis at 8 weeks, since when it had a poor appetite and did not finish the feeds. Vomiting for 3 days before admission to hospital. Stools normal. Losing weight for 3 weeks before admission.

APPENDIX F.

STATISTICAL DATA.

(a) Standard Deviation and Standard Error.

The Standard Deviation and the Standard Error were calculated for the free and total acidity in each age period (3 to 4 weeks, 5 to 12 weeks, 13 to 26 weeks, 27 to 39 weeks, and 40 to 52 weeks), in the 5 groups of cases examined, i.e. normals, acute primary gastro-enteritis, acute parenteral infections, pyloric stenosis and infantile atrophy.

The Standard Deviation (σ) and the Standard Error were found according to the formulae

$$\sigma = \sqrt{\frac{\text{sum of squares of observations}}{\text{number of observations}} - (\text{means of observation})^2}$$

and Standard Error $= \dfrac{\sigma}{\sqrt{\text{number of observations}}}$

These results were expressed in the text as "(mean of observations) $\pm$ Standard Error" e.g. average free acidity in normal infants aged 5 to 12 weeks was 12.88 ± 2.50 mN.

(b) Students "t" test.

i.e. $t = \dfrac{\text{difference between the means}}{\text{Standard Deviation of the difference between the means}}$

If m_1 and m_2 are the means of the two groups being compared, and n_1 and n_2 are the number of observations that have been averaged to obtain m_1 and m_2 respectively and if σm_1 = Standard Deviation of m_1 (i.e. Standard Error of the distribution averaged to obtain m_1) and similarly m_2 = Standard Deviation of m_2, then

Standard Deviation (σ) of difference between the means $= \sqrt{\sigma m_1^2 + \sigma m_2^2}$

$$\text{and } t = \frac{m_1 - m_2}{\sqrt{\sigma m_1^2 + \sigma m_2^2}}$$

Degrees of freedom (d.f) = $(n_1 + n_2 - 2)$.

From tables of "t", the probability (P) of the observed difference being due to chance were obtained.

e.g. $t = 3.01$, d.f. $= 27$, $P = \frac{1}{740.}$

In assessing the significance of P, if the value of the fraction is $\frac{1}{20}$ or less, then the observed difference is generally held to be significant.

Table 1. Free Acid. Students "t" test.

1:2	M_1	M_2	diff.	σm_1	σm_2	σdiff	d.f.	t.	P= 1/
Normal: A.P.G.E.									
3-4 wks.	2.13.	0	2.13	1.06	0	1.06	4	2.01	16
5-12 "	12.88	11.38	1.50	2.50	3.53	4.33	22	0.35	2
13-26"	14.46	5.81	8.65	1.67	2.33	2.87	27	3.01	740
27-39"	16.90	2.92	13.98	1.51	1.73	2.30	7	6.08	3332
40-52"	19.85	0	19.85	1.02	0	1.02	5	19.46	X
Normal: Parent-eral.									
3-4 wks.	2.13	0	2.13	1.06	0	1.06	2	2.01	10
5-12 "	12.88	8.39	4.49	2.50	3.62	4.40	15	1.02	5
13-26"	14.46	7.06	7.40	1.67	2.75	3.22	11	2.30	47
27-39"	16.90	7.00	9.90	1.51	2.34	2.79	9	3.55	344
40-52"	19.85	3.50	16.35	1.02	2.47	2.67	4	6.12	525
Normal: Pyloric Stenosis.									
3-4 wks.	2.13	12.17	10.04	1.06	4.64	4.76	5	2.11	21
5-12 "	12.88	20.86	7.98	2.50	5.43	5.98	13	1.33	8
Normal: Infant-ile Atrophy.									
5-16 wks.	13.05	18.28	5.23	2.17	3.50	4.12	18	1.27	9

A.P.G.E. = Acute primary gastro-enteritis.
X = highly significant.

Table 2. Total Acid. Students "t" test.

1:2	M_1	M_2	diff.	σm_1	σm_2	σ diff	d. f.	t	P= 1/
Normal: A.P.G.E.									
3-4 wks.	14.18	25.50	11.32	2.68	1.77	3.21	4	3.53	80
5-12 "	33.00	37.84	4.84	2.68	4.34	5.10	22	0.95	5
13-26"	33.74	38.19	4.45	2.30	4.54	5.09	27	0.87	4
27-39"	31.17	31.67	0.50	2.48	4.32	4.98	7	0.10	1
40-52"	37.75	30.67	7.08	4.13	5.89	7.19	5	0.98	5
Normal: Parent-eral.									
3-4 wks.	14.18	0	14.18	2.68	0	2.68	2	5.29	58
5-12 "	33.00	41.94	8.94	2.68	5.30	5.94	15	1.51	12
13-26"	33.74	25.00	8.74	2.30	3.59	4.26	11	2.05	33
27-39"	31.17	37.19	6.02	2.48	5.36	5.91	9	1.02	5
40-52"	37.75	24.00	13.25	4.13	5.66	7.01	4	1.96	16
Normal: Pyloric Stenosis.									
3-4 wks.	14.18	47.17	32.99	2.68	6.87	7.37	5	4.48	311
5-12 "	33.00	64.71	31.71	2.68	7.77	8.15	13	3.89	X
Normal: Infant-ile Atrophy.									
5-16 wks.	33.72	47.10	13.38	2.37	5.30	5.81	18	2.30	59

A.P.G.E. = Acute primary gastro-enteritis
X = highly significant.

(c) Percentile Curves.

The time of maximum secretion was estimated by plotting the percentile distribution and deducing the Median, and the Semi-interquartile Range, the estimate being expressed as (Median $\pm$ Semi-inter-quartile Range). The method is only strictly valid when the distribution is symmetrical, vide Graph I, though a fairly close approximation to symmetry is found in all cases studied. In view of the limited number of cases, more rigorous statistical tests were not considered to be warranted; reference is particulary made to Graph IX, the most assymetrical figure in the present series where the first quartile has a range of 60 to 90 minutes, and the second quartile only from 90 to 108 minutes.